A Canine Window into Human Evolution: Brain Morphology, Asymmetry, and Plasticity

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Sophie Barton

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Abstract

Understanding how brains evolve requires a system in which selective history, brain size and structure, skull morphology, and behavioral specialization can be measured directly, dissociated from one another, and compared across differentiable lineages. The domestic dog (*Canis familiaris*) provides exactly this. Through a combination of natural and artificial selection, dogs have evolved extraordinary variation in skull morphology, brain anatomy, and behavior within a single species, and they can be studied using the same neuroimaging methods applied to humans. In this dissertation, I use dogs as a living model system to test biological principles of brain evolution that are directly relevant to the human lineage. In Chapter 2, I show that variation in skull shape significantly predicts regional gray matter volume, demonstrating that selection on skull morphology can reshape brain organization. In Chapter 3, I characterize widespread neuroanatomical asymmetry in the canine brain and find that lateralization does not scale with brain size, suggesting it is not simply a byproduct of encephalization but may instead reflect selection on lateralized behaviors. In Chapter 4, I compare modern breed dogs, which were intensively selected for cooperative learning, with premodern dogs that underwent far less artificial selection. Modern breeds show cortical expansion linked to trainability, while premodern dogs show amygdala enlargement linked to fear. In Chapter 5, I extend this comparison to white matter and find that modern breeds exhibit greater fractional anisotropy, altered connectome topology, and fractional anisotropy patterns that predict trainability. In Chapter 6, I compare Labrador retrievers that vary in breeding lineage and training history and find evidence for experience-dependent plasticity in working dogs but no innate neuroanatomical differences between non-working dogs from different lineages, suggesting that selection may favor neuroplasticity itself rather than canalization of specific skills. Altogether, this dissertation demonstrates that even over short evolutionary timescales, selection can substantially reshape brain structure, and that

the domestic dog offers a powerful window into the principles governing brain evolution in species that shares our anthropogenic niche.

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Acknowledgements

During my early childhood, I had the immense privilege of watching my mother pursue a PhD. She regularly brought me to campus, and while she wrote her dissertation, my brother and I sat with her in her office and wrote mini “books” about the natural world. It was through this experience that I grew to love academia, but more importantly, the pursuit and sharing of knowledge. During my mum’s graduation, as I playfully placed her doctoral tam on my head, it dawned on me that I wanted to earn my own PhD one day. Later, when I was a young teenager, my mum became a professor. She taught me how her job worked, and I saw how much she thrived in her occupation. I decided that I wanted to share her title, Professor Barton, in no small part because she showed me how rewarding and meaningful being a professor can be. Therefore, I extend my deepest thanks to my mum, who inspired me and supported my dreams with an unwavering belief that I could achieve my goals.

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Chapter 1 Introduction

1.1 Reconstructing Human Brain Evolution

Brain evolution is central to the origin of our species. Since diverging from our last common ancestor with chimpanzees and bonobos approximately 6-7 million years ago (Besenbacher et al., 2019; Kumar et al., 2005), the hominin lineage acquired a suite of neural adaptations (Hecht et al., 2015a; Preuss, 2011; Van Den Heuvel et al., 2023) that enabled their expansion into diverse environments across the African continent and later the rest of the globe (Groucutt et al., 2015; Scerri et al., 2018; Zeller et al., 2023). In particular, the genus Homo is hypothesized to have evolved neural mechanisms that enhanced the transmission and inheritance of cultural information (Stout & Hecht, 2017), resulting from cortical expansion (Buckner & Krienen, 2013) and modification of pre-existing brain adaptations (Platt et al., 2016). Such changes appear to have enabled the emergence of cumulative culture (Muthukrishna et al., 2018), which is a defining feature of our species (Boyd et al., 2011).

Yet our ability to reconstruct this evolutionary history is severely constrained. Hominin endocrania and endocasts provide only a coarse proxy for brain organization, as external cortical morphology is largely independent of internal neural architecture (Alatorre Warren et al., 2019), rendering important neural features such as connectivity completely invisible to the fossil record. While this can be circumvented by investigating the brains of our modern great ape relatives, these studies are limited by the long divergence time between great apes and humans, the possibility that modern ape lineages have themselves diverged considerably from our last common ancestor (Almécija et al., 2021; Staes et al., 2019), and the difficulty of determining which neural differences between humans and apes correspond to which behavioral differences (Logan et al., 2018). The highly plastic nature of the human brain further complicates the matter of distinguishing innate adaptations from specializations resulting from experience (Buckner & Krienen, 2013; Hecht, 2018). These issues call for the use of a model system to study relevant patterns of brain evolution in a controlled manner with high temporal resolution (i.e., the capacity to sample brain organization at many points along an evolutionary trajectory, rather than only at its endpoints).

1.2 A Living Comparative Framework

The domestic dog (*Canis familiaris*) offers an unexpected solution to these problems. Like humans, dogs evolved to inhabit the anthropogenic environment, but this process unfolded on a timescale that we can interrogate directly through comparisons of differentiable, extant lineages. Sometime between 40,000 and 15,000 years ago, dogs diverged from a now-extinct ancient wolf population (Bergström et al., 2022; Freedman et al., 2014) and were progressively shaped by the demands of living alongside humans. Crucially, this process has multiple, separable phases: an early commensal transition in which proto-dogs adapted to human settlements (Coppinger & Coppinger, 2001); subsequent periods of modest, function-driven artificial selection (Brassard et al., 2022; Hansen Wheat et al., 2020); and an intense phase of selective breeding over the past 200 years that has produced the highly derived modern breeds we recognize today (Worboys et al., 2018). Because these phases differ in their selective pressures and their effects on brain and behavior, they provide a natural comparative design for dissociating what cannot be dissociated in the hominin record. Specifically, they can inform what happens to brain structure and behavior when selection acts on socially learned skills and on brain size itself, and how these effects vary across populations and lineages.

It is important to note at the outset that this framework does not assume that humans are a domesticated species in the same sense as dogs. Whether dogs and humans share a domestication syndrome is a debated question that will not be pursued here (Hecht, Barton, et al., 2023; Sánchez-Villagra & Van Schaik, 2019). Rather than asking whether the two species arrived at the same endpoints, the goal of this dissertation is to ask whether dogs can illuminate the biological principles that govern how brains evolve in human environments.

1.3 Convergent Brain Evolution

Dog brains have several features that make them relevant to human brain evolution. Although the last common ancestor of carnivorans and primates lived approximately 94 million years ago (Kumar et al., 2017)—and despite the fact that primates are genetically more closely related to rodents than to carnivorans—primate and carnivoran brains have independently evolved an enlarged, gyrified neocortex, unlike conventional rodent models (Kaas, 2013). Within the carnivorans, canids show the most extreme

encephalization (Finarelli & Flynn, 2009) and have convergently evolved a temporal lobe (Bryant & Preuss, 2018) that in awake fMRI studies performs socio-perceptual functions analogous to those of the human temporal lobe (Boch et al., 2023; Cuaya et al., 2016; Thompkins et al., 2018).

Canids also show expansion of the frontal and prefrontal cortex that is second only to primates among mammals (Bush & Allman, 2004). Notably, within carnivoran species, the prefrontal cortex is particularly enlarged in highly social Canis species, which suggests that they may have undergone social brain expansion in a manner similar to the hominin lineage (Finarelli & Flynn, 2009; Radinsky, 1969). Canids are therefore a particularly well-positioned comparative model for investigating how selection for social cognition shapes brain organization.

Another notable shared feature of human and canine brains are their extended periods of postnatal cognitive and neural development. In both species, there is protracted development of the myelin sheaths of axons that boost signal transmission, with the regions showing the most protracted development including frontal, temporal, and parietal regions (Fox, 1971b), as is the case in humans (Miller et al., 2012). In dogs, evidence from EEG suggests that the central nervous system is not fully mature by 12 months (Pellegrino & Gómez Álvarez, 2023; Reicher et al., 2021), which is after sexual maturity for many dogs. Recent studies of cognitive development in dogs support this finding, suggesting that dogs have an adolescent period (Bray et al., 2021).

Of course, there are still some important differences between the human and dog brain. Perhaps the most significant difference is that the human brain is far more massive in both absolute and relative size than the dog brain. To fit the entire volume of the brain within the neurocranium, the human brain is far more gyrified or folded than the dog brain (Fernández & Borrell, 2023). Furthermore, due to the almost 5-fold variation in body size between the smallest and largest dogs (Hecht et al., 2019), dog brains vary far more in absolute and relative size than human brains. This is thought to contribute to the neuroanatomical diversity observed in dog brains (Hecht et al., 2021), which also show focal adaptations related to different temperaments and behaviors across lineages (Hecht et al., 2019).

Far from being detrimental, many differences between human and dog brains can be leveraged as strengths when studying human-relevant brain evolution in dogs. Because canine brains are

intermediate in size between a rodent and a human brain, they have just enough complexity to draw meaningful parallels with humans but are simpler than human brains and thus offer a more direct path to mapping brain-behavior relationships. Furthermore, the large variation in brain size within dogs means that questions regarding brain scaling can be asked within a single species with a common genetic background. Lastly, the evolved neural diversity within dogs allows for precise brain-behavior mapping of many divergent behaviors.

1.4 Parallels in Social Cognition and Behavior

There are two major parallels in the evolutionary histories of dogs and humans that make dogs especially good models for studying questions relevant to human evolution. First, like humans, dogs evolved to live in human social groups and networks. Human relationships with their companion dogs resemble relationships with a human child or best friend (Turcsán et al., 2025). Critically, this orientation toward humans is not simply a product of pet-keeping. Even dogs who live outside of human homes still incorporate humans as key nodes in their social networks (Bhattacharjee & Bhadra, 2020). Indeed, humans appear to function as the primary social partners of dogs more so than other dogs. Companion dogs form stronger attachment bonds to human owners than to conspecific housemates, and use humans rather than other dogs as a secure base for exploration (Sipple et al., 2021). Consequently, across the spectrum of dog populations, the human social environment has been the primary context in which selection has acted on canine cognition and behavior, mirroring the social context that shaped the evolution of our own species.

Second, not only do dogs live within human social environments, but they also possess the sociocognitive toolkit to adeptly navigate them. These abilities are not unique to dogs but reflect a broader convergence between canids and primates. They have both evolved similar facial expressions (Bolwig, 1964; Fox, 1971), suggesting that the social demands of group living have convergently shaped analogous communicative systems across distantly related lineages. Within this canid heritage, dogs retain a suite of advanced sociocognitive abilities, including gaze following (Range & Virányi, 2011), sensitivity to human pointing gestures (Udell et al., 2008), and cooperative problem solving (Range & VirÃ¡nyi, 2015), that also evolved in the human lineage. Notably, many of these abilities did not originate

through domestication but were already present in ancestral canids that were shaped by the demands of living in complex social groups. Domestication appears to have refined and redirected canine sociocognitive abilities toward human social partners specifically (Range & Virányi, 2015).

1.5 Chapter Previews

The chapters that follow each address a question about how brains evolve to live in the anthropogenic niche that cannot be resolved by the hominin fossil record or living great ape relatives alone. Together they exploit the comparative design that dog diversity uniquely affords -- a single species in which selective history, skull morphology, brain size, and behavioral specialization vary independently across differentiable, extant lineages, and in which all variables can be measured directly using the same neuroimaging methods applied to humans. Each chapter isolates one dimension of this variation to test a biological principle of brain evolution that is directly relevant to the hominin lineage but otherwise intractable.

1.5.1 Chapter 2 Preview

Anatomically modern Homo sapiens (AMHS) can be distinguished from archaic humans based on differences in skull shape (Zollikofer, 2012). Specifically, AMHS are characterized by having a more globular neurocranium and a retracted face (Lieberman et al., 2002). Approximately 300,000 years ago, early members of the *H. sapiens* lineage, most prominently represented by the Jebel Irhoud specimens from Morocco (Hublin et al., 2017), already possessed absolute brain volumes that fall comfortably within the range of present-day humans (roughly 1,200–1,500 cm^3) (Neubauer et al., 2018). While their faces were orthognathic (flat rather than projecting), their endocranial shape remained decidedly archaic (Hublin et al., 2017). Brain size, in other words, had reached its modern plateau well before brain shape followed suit. Analyses of the fossil record indicate that the globular configuration of the brain characteristic of living humans evolved approximately 100,000 to 35,000 years ago (Neubauer et al., 2018; Zollikofer et al., 2022).

This reshaping of the human skull was accompanied by changes in brain shape and internal organization. The parietal lobe dilated (Bruner, 2004), possibly due to expansion of the precuneus (Bruner

et al., 2015) and deep parietal regions (Bruner, 2015). The frontal lobe widened, which was potentially enabled by the shortening of the facial block and reduction of the temporal muscle (Bruner & Holloway, 2010). Meanwhile, the cerebellum expanded and became more rounded (Neubauer et al., 2018).

Unfortunately, any further neuroanatomical alterations, such as changes to the sizes of brain regions and connections between them, are invisible to the fossil record. This issue can be circumvented by adopting a model organism system. Rodents bred for different brain sizes and shapes have been traditionally used for this purpose, but their elongated skulls do not recapitulate the true globular shape of the human skull and therefore only lend limited insights.

It is here that dogs offer a surprisingly powerful comparative framework. Artificial selection has favored extraordinary variation in canine skull shape, from the dolichocephaly (long-snouted, narrow cranium) of greyhounds to the brachycephaly (short-faced, wide cranium) of pugs. This range of morphological variation exceeds what is seen across the entire hominin fossil record. Crucially, this variation is produced not by changes in absolute brain volume, but by shifts in the spatial proportions and curvature of the braincase, closely paralleling the decoupling of size and shape observed in *H. sapiens* evolution (Neubauer et al., 2018).

In brachycephalic breeds in particular, the cerebral hemispheres rotate ventrally and the skull vault rounds dorsally (Selba et al., 2021) in a manner that produces striking geometric similarities to the globular profile of AMHS — a convergence that, while not implying shared selective pressures, provides a tractable living model for studying how changes in basicranial flexion, facial reduction, and vault curvature interact mechanically and developmentally. Because dog breeds can be compared across controlled genetic backgrounds, imaged with modern neuroimaging tools, and studied across ontogenetic stages, they allow one to isolate variables, such as the relationship between vault roundness and underlying cortical organization, that are simply inaccessible in the paleoanthropological record. In this sense, the domestic dog serves not merely as an anatomical curiosity, but as a uniquely accessible window into the developmental and biomechanical logic of a major transformation in human evolutionary history.

Chapter 2 uses this framework to investigate how regional gray matter volume covaries with skull shape in dogs to inform how the human brain might have changed as it became more globular.

1.5.2 Chapter 3 Preview

Ever since the neurologist Paul Broca wrote that "…nous parlons avec l'hémisphère gauche" (Broca, 1865), which translates to "we speak with the left hemisphere," there has been a strong focus on the asymmetrical organization of the human brain. Because this asymmetry was first appreciated in the context of language, it was once assumed that it was a human-specific adaptation (Güntürkün et al., 2020). It is now clear that brain lateralization occurs in a wide range of distant taxa and is a general feature of brain organization (Rogers et al., 2013). Even still, how and why brain lateralization evolves remains an unresolved question (Ocklenburg & Güntürkün, 2017).

One major hypothesis is that brain asymmetry has evolved repeatedly across many species because it is adaptive (Vallortigara & Rogers, 2005). For example, it might allow the two halves of the brain to carry out processes in parallel (Dadda & Bisazza, 2006; Rogers et al., 2004) and/or divide labor between the hemispheres, thus increasing the amount of functional neural "real estate" available (Rogers, 2021). Alternatively, it has been proposed that brain lateralization is a result of brain scaling (Ringo et al., 1994), and/or subtle developmental differences between the two hemispheres (Bishop, 2013), and that it need not be functionally advantageous (Nadeau, 2010).

Among primates, humans show especially pronounced patterns of neural asymmetry (Gómez-Robles et al., 2016; Neubauer et al., 2020), and this could be because our brains are exceptionally large. Yet many of these asymmetries are directionally consistent at the population level, which argues against a purely stochastic developmental account, which would predict random left-right variation across individuals (Güntürkün et al., 2020). Interestingly, altered or weakened asymmetry of the language network is associated with language impairments in several neurodevelopmental disorders, including schizophrenia (Zimmermann et al., 2024), autism (Postema et al., 2019), and dyslexia (Verhelst, 2025). This not only suggests that asymmetry may be generally adaptive for language performance, but also that altered asymmetry may play a direct role in neurodevelopmental disorder etiology (Bishop, 2013). Yet the clinical literature cannot on its own resolve the deeper evolutionary question of whether brain lateralization in humans reflects selection for something like complex skills, a more general consequence of brain scaling, or some interaction between the two.

To directly test these ideas, an ideal model system would exhibit substantial variation in brain size across differentially selected lineages. Once again, dogs are unusually well-suited to the task of informing evolutionary principles directly relevant to the human lineage. Their almost five-fold variation in brain size (Hecht et al., 2019) permits the investigation of whether asymmetry scales with brain size across members of the same species. Furthermore, because different breeds were intentionally selected for different skilled behaviors rather than for brain size per se, dogs also allow these two potential drivers of lateralization to be partially decoupled.

Chapter 3 uses structural neuroimaging to establish what patterns of asymmetry are present in the dog brain, to examine whether asymmetry scales with increasing brain size, and to investigate if asymmetry is associated with behavioral specializations.

1.5.3 Chapter 4 Preview

Humans are a species that specialize in the acquisition, use, and spread of cultural knowledge. This is enabled by our derived social learning abilities (Boyd et al., 2011), including high-fidelity imitation and over-imitation, which are rooted in neuroanatomical adaptations specific to the human lineage. For example, humans engage in high-fidelity imitation, which involves a derived fronto-parietal-temporal circuit that distinguishes humans from other primates (Hecht et al., 2013). Humans also have an expanded portion of the cerebral cortex called the association cortex, which is especially involved in learned behaviors (Buckner & Krienen, 2013).

Not only did humans evolve adaptations for social learning, but they also evolved the ability to teach others (Csibra & Gergely, 2011). Teaching is rare across taxa and is thought to evolve in circumstances where the cost of independent learning is high and knowledge is difficult to acquire alone (Thornton & Raihani, 2010). While the neural substrates of teaching are less known, emerging evidence suggests that teaching engages a suite of social brain regions, particularly those implicated in mentalizing and theory of mind (Vélez et al., 2023), and that the act of knowledge transmission is associated with neural coupling between teacher and learner (Li et al., 2024; Nguyen et al., 2022)

Like humans, dogs are deeply embedded in a cultural learning environment, but unusually, this environment is an interspecific one. While humans have domesticated several species that interact closely with them, dogs are arguably unique in the extent to which they have been selected for cooperative social learning from human partners, making them a distinctive case of convergent social evolution (Pongrácz & Dobos, 2025b). This cultural embedding appears to have left a mark on dogs' capacity to learn specifically from human teachers. Modern dog breeds that were historically selected to work in close coordination with human handlers, such as herding and gun dogs, utilize human demonstration more effectively than more independent breeds (Pongrácz & Dobos, 2025a). This effect extends to communicative signals. Cooperative breeds show greater sensitivity to human verbal cues during observational learning, responding to both ostensive and neutral human speech during demonstration (Dobos & Pongrácz, 2024). Notably, more independent breeds learn better from a conspecific dog demonstrator than from a human, suggesting that recent selection has changed the preferred social source from which learning occurs in more cooperative breeds (Dobos & Pongrácz, 2024).

Dogs offer an excellent opportunity to investigate how selection for social learning from human instructors drives neural change. Given that different breeds and lineages vary in whether they have been selected for human-directed social learning, or “trainability”, but all live in the human niche, they are a promising model for pinpointing how the demands of being taught shape the brain. Specifically, it would be informative to contrast modern breed dogs, which were intensively selected to learn complex tasks from humans (Turcsán et al., 2011), and premodern dogs, which underwent far less artificial selection (Brassard et al., 2022; Hansen Wheat et al., 2020). Modern breed dogs are known for being more trainable than premodern dogs (Smith et al., 2017; Turcsán et al., 2011) and other research has found that trainability is heritable (MacLean et al., 2019), meaning that modern breed dogs may have evolved neural adaptations for learning from people. Furthermore, modern breed dogs have relatively larger brains than premodern dogs (Garamszegi et al., 2023), which would allow one to test the hypothesis that encephalization drives the evolution of social learning abilities.

Chapter 4 will apply this framework to investigate differences in regional gray matter volume in modern breed and premodern dogs and how they relate to trainability. The aim is to test whether encephalization, and consequently expansion of the cerebral cortex, enhances trainability.

1.5.4 Chapter 5 Preview

Most neuroimaging studies, in both humans and dogs, have focused on gray matter, leaving the white matter pathways that determine the speed, efficiency, and integration of communication across circuits comparatively understudied (Filley & Fields, 2016; Grajauskas et al., 2019). Similarly, evolutionary neuroscience as a field has been slower to characterize white matter than gray matter, as comparative tractography is a relatively recent and still niche endeavor (De Schotten et al., 2019; Rilling, 2014), and white matter atlases exist for only a handful of species (Bryant et al., 2020; Feng et al., 2017; C. Liu et al., 2020).

In comparison to our closest living great ape relatives, humans show several specializations in white matter organization. The human connectome exhibits an evolutionary shift toward greater investment in the white matter pathways linking multimodal association cortex areas of the temporal, parietal, and inferior frontal cortices, with these connections making a disproportionate contribution to global network integration (Ardesch et al., 2019). One major white matter pathway, the superior longitudinal fasciculus (SLF) shows greater connectivity to the dorsolateral prefrontal cortex in humans compared to chimpanzees, which may support imitative abilities in humans (Hecht et al., 2015). Another major white matter tract, the arcuate fasciculus, implicated in language, is substantially expanded in the human temporal lobe relative to chimpanzees (Rilling et al., 2008).

Although comparisons with modern great apes are highly informative, they fail to capture the patterns of white matter change that occurred in the hominin lineage in the past 6-7 million years. Fortunately, given that dogs show enormous variation in brain size and selective pressures (Hecht et al., 2019), they offer a natural experiment into how white matter evolves. As discussed previously, they may be especially useful for investigating questions regarding neural adaptations for learning socially from humans.

Chapter 5 extends the modern breed/premodern dog comparison to white matter organization using diffusion MRI and graph-theoretical analyses.

1.5.5 Chapter 6 Preview

What is similar between a border collie gathering a flock of sheep and a shepherd issuing verbal cues for her to do so? Both animals are performing skilled behaviors (herding and language, respectively) that emerge through some combination of innate predisposition and lifetime experience (Coppinger & Coppinger, 2001; McMurray, 2016). In humans, disentangling the contributions of genes and experience to skilled behaviors like language and tool use is exceptionally difficult (McAdams et al., 2023). Language is acquired universally across cultures (Fitch, 2010), which hints at a strong biological foundation, yet the environments in which it is learned vary enormously (Ochs & Schieffelin, 1984), making it nearly impossible to hold one factor constant while manipulating the other (McMurray, 2016). What is needed is a system in which individuals share a genetic background but differ in their experiential demands or share experiential demands but differ in their selective history.

Working Labrador retrievers are an ideal model system for investigating inherited and acquired adaptations for skilled behaviors. Labrador retrievers are the most popular working dog breed, and they are used to perform a variety of skills, including hunting, scent detection, and service work. They differ in their selective history: hunting line Labradors are bred primarily for hunting, but are sometimes used for scent detection, whereas service-line dogs are bred solely for service work. Within the service dog population, there are individuals who are released from programs and become companion dogs, allowing for a comparison between dogs of identical genetic background whose experiential demands have diverged. This means that within a single breed, it is possible to hold genetics approximately constant while varying working experience, and to hold experience approximately constant while varying selective history, which are the two comparisons necessary to disentangle innate from acquired adaptation.

Chapter 6 will compare structural and diffusion MRI data of hunting line Labradors trained for hunting and scent detection, with service line Labradors trained for service work or released from service work and living their lives as non-working companion dogs.

1.6 Dissertation Aims

The chapters of this dissertation use domestic dogs as a living experimental system to test five biological principles of brain evolution that the hominin fossil record poses but cannot resolve: whether skull morphology drives neuroanatomical reorganization; whether structural asymmetry is a consequence of encephalization or a target of selection; whether selection for social learning drives cortical expansion; how white matter architecture changes in response to selection for social learning; and how innate and acquired neural adaptations for learned skills can be disentangled. Each question is addressed in a species where the relevant variables can be measured directly, dissociated from one another, and compared to the human neuroimaging literature using identical methods, offering a window into the principles of brain evolution that the fossil record, and our closest living relatives, cannot provide.

Chapter 2 Covariation of Skull and Brain Morphology in Domestic Dogs

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2.1 Abstract

Despite their distinct embryonic origins, the skull and brain are highly integrated. Understanding the covariation between the skull and brain can shed light on anatomical, cognitive, and behavioral traits in extant and extinct species. Domestic dogs offer a unique opportunity to investigate skull–brain covariation due to their diverse skull morphologies and neural anatomy. To assess this question, we examined T2-weighted MRI studies of 62 dogs from 33 breeds, plus an additional 17 dogs of mixed or unknown breeds. Scans were opportunistically collected from a veterinary teaching hospital of dogs that were referred for neurological examination but did not have grossly observable structural brain abnormalities. As the neurocrania of dogs become broader and shorter, there is a significant decrease in the gray matter volume of the right olfactory bulb, frontal cortex, marginal gyrus, and cerebellum. On the other hand, as the neurocrania of dogs become narrower and longer, there is a significant decrease in the gray matter volume of the olfactory bulb, frontal cortex, temporal cortex, amygdala, hypothalamus, hippocampus, periaqueductal gray, cerebellum, and brainstem. Selective breeding for specific skull shapes may impact canine brain anatomy and function.

2.2 Introduction

Because the brain is housed within the neurocranium, it must coevolve and codevelop with the skull (Hanken and Thorogood1993; Richtsmeier and Flaherty 2013). This is no small feat, given that neural and cranial tissue are derived from distinct embryonic germ layers and serve disparate functions (Noden and Trainor2005; Stiles and Jernigan 2010; Vyas, Nandkishore, and Sambasivan 2020). Several animal species have been leveraged to under-stand the covariation between the brain and skull, including mice (Barbeito-Andrés, Gonzalez, and Hallgrímsson 2016), pigs (Ritter et al. 2023), cichlid fishes (Conith, Hope, and Albertson2023), and frugivorous bats (Rojas, Borrero-Ospina, and Murillo-García 2022). Domestic dogs offer a unique opportunity to further address the question of how brain and skull morphology interact. As early domestic dogs transitioned from an ancestor related to modern gray wolves to currently recognized dog breeds, their skulls became shorter and their snouts became wider (Galetaet al. 2021). More recent artificial selection has produced an exceptionally wide range of skull morphotypes (Brassard et al.2022; Drake and Klingenberg 2010; Schoenebeck and Ostrander2013) as well as considerable variation in neuroanatomy (Hechtet al. 2019). Given the increasing usage of dogs as model organisms for genetics (Parker, Shearin, and Ostrander 2010) and neuroscience research (Bunford et al. 2017), they are ideally suited to uncovering relationships between skull and brain morphology.

Major dog skull morphotypes can be measured and distinguished by cephalic index, which is the ratio of skull width to skull length (Helton 2009). Brachycephalic dogs have a very high cephalic index value, meaning that their skulls are short and wide. On the other hand, the skulls of dolichocephalic dogs have a very low cephalic index, meaning that their skulls are long and narrow. There are also mesocephalic (mesaticephalic) dogs, with intermediate cephalic index values (Miller, Christensen, and Evans 1964).

Previous research has found that dogs with more brachycephalic skull shapes have a smaller cerebral cortical to lateral ventricular volume ratio than dogs with more dolichocephalic skull shapes (Pilegaard et al. 2017). The dorsoventral dimensions of the brain and lateral ventricles are larger in brachycephalic dogs than in mesocephalic and dolichocephalic dogs (Doiche et al. 2022). Likewise, the brain is wider in brachycephalic dogs (Selba et al.2020). Additionally, the position of the olfactory bulb is

more ventral in brachycephalic dogs (Alvites et al. 2023) and differs in shape (Selba et al. 2020). This may be related to the fact that the rhinencephalic region containing the olfactory bulb is reduced in dogs with high cephalic index values, as measured using digital dog endocasts (Czeibert et al. 2020).

The covariation between skull and brain shape in dogs may have some functional consequences, as certain behavioral phenotypes are significantly associated with dog skull shape. Dogs with ahigh cephalic index (more brachycephalic) establish eye contact faster with an unfamiliar experimenter (Bognár et al. 2021). They also gaze longer at pictures of human and canine faces (Bognár,Iotchev, and Kubinyi 2018) and follow human pointing gestures more accurately (Gácsi et al. 2009). On the other hand, dogs with low cephalic index values (more dolichocephalic) are more prone to chase small animals (McGreevy et al. 2013), although dogs with brachycephalic head shapes are more inclined to chase prey-like toys (Stone et al. 2016). Additionally, dolichocephalic dogs behave more fearfully towards human strangers (McGreevyet al. 2013), as well as a startling metallic noise and the sudden appearance of a dummy (Stone et al. 2016). Behavioral differences associated with skull shape are even observed in juvenile dogs during conspecific play—brachycephalic puppies engage in more head sniffing, pouncing, and body biting (Kerswell et al. 2010).

However, it is difficult to relate these behavioral traits to skull–brain covariation, as little is known about how brain regions other than the olfactory bulb might covary with skull shape. There is initial evidence from Hecht et al. (2019) that neurocephalic index, which is the ratio of the neurocranium width to neurocranium length, is associated with the anatomy of structural brain networks implicated in dog breed historical working behavior. But the relationship between skull shape and individual brain regions within those networks was not examined in that study. Further research is necessary to address the relationship between skull shape and regional brain anatomy—especially for the purpose of understanding why skull shape covaries with certain behaviors in dogs.

The present study sought to address this gap in the literature by investigating whether regional gray matter volume covaries with neurocephalic index in a previously published MRI dataset of 62 purebred dogs of 33 different breeds (Hecht et al. 2019), with an additional 17 dogs of mixed or unknown breed status. We used neurocephalic index as a measurement of skull shape, rather than cephalic index,

because the field of view for the images in this dataset did not include the entire skull. However, it should be noted that neurocephalic index is positively correlated with cephalic index (Hecht et al. 2019) and represents internal anatomy, which is potentially more relevant to brain morphology than external skull shape. We hypothesized that there would be a significant correlation between regional gray matter volume and neurocephalic index—that is, that variation in skull shape would significantly predict variation in the size of gray matter regions throughout the brain. Furthermore, based on prior research, we hypothesized that dogs with a high neurocephalic index value (short and wide skull) would have significantly smaller olfactory bulbs than other dogs in the dataset.

2.3 Methods

2.3.1 Subjects

Subjects for the study came from a previously published, opportunistic dataset (Hecht et al. 2019) containing T2-weighted MRI scans from 62 purebred dogs representing 33 different breeds. In the present analysis, we also included an additional 17 dogs of mixed or unknown breeds that were not included in our earlier dataset, for a total of 79 dogs (see Table 1). The data were collected at the University of Georgia's Veterinary Teaching Hospital in Athens, GA. All dogs in the dataset underwent MRI scans for medical reasons but were not diagnosed with any observable structural brain abnormalities by a veterinary neurologist (M.K.).

ID	Breed	Sex	Age	Body mass (kg)	Cephalic index (from database)	Neurocephalic index
1	Basset Hound	Male	4.02	28.10	51.89	74.1
2	Beagle	Male	14.29	17.00	61.82	73.8
3	Beagle	Male	4.04	11.70	61.82	76.4
4	Beagle	Male	ND	28.50	61.82	84.8
5	Beagle	Male	4.00	8.30	61.82	82.4
6	Beagle	Male	1.69	28.50	61.82	77.8
7	Bichon Frise	Male	9.01	9.30	61.51	80.4
8	Border Collie	Male	6.05	28.20	54.38	65.2

9	Border Collie	Male	5.56	20.60	54.38	65.3
10	Boston Terrier	Male	11.90	12.50	92.62	90.2
11	Boston Terrier	Male	5.80	8.90	92.62	89.7
12	Boxer	Male	8.08	31.75	67.19	67.6
13	Boxer	Male	5.01	34.20	67.19	67.3
14	Boxer	Female	10.72	31.75	66.28	83.2
15	Boxer	Male	9.25	40.80	67.19	69.7
16	Bulldog	Male	1.00	16.78	90.18	74.0
17	Bulldog	Male	4.42	30.00	90.18	77.1
18	Cavalier King Charles Spaniel	Female	0.47	3.20	76.77	81.4
19	Cavalier King Charles Spaniel	Female	0.47	14.50	76.77	92.0
20	Cocker Spaniel	Female	6.38	18.10	61.01	75.4
21	Dachshund	Female	11.30	4.90	51.76	79.2
22	Dachshund	Female	6.56	6.40	51.76	77.3
23	Dachshund	Male	7.83	5.60	49.59	81.2
24	Dachshund	Female	1.81	5.30	51.76	81.1
25	Doberman Pinscher	Female	4.67	29.80	46.96	62.3
26	English Pointer	Male	7.34	27.30	ND	74.2
27	German Shorthaired Pointer	Female	6.17	27.00	48.3	73.4
28	Golden Retriever	Male	10.01	39.80	56.52	68.9
29	Golden Retriever	Male	6.01	42.20	56.52	70.1
30	Golden Retriever	Male	11.01	34.90	56.52	68.0
31	Greyhound	Female	7.52	36.70	45.83	64.8
32	Greyhound	Male	3.82	37.10	46.84	65.1
33	Greyhound	Female	2.20	36.00	45.83	66.5
34	Jack Russell Terrier	Male	ND	14.00	59.28	80.1

35	Keeshond	Male	7.17	21.60	60.18	71.0
36	Labrador Retriever	Male	9.72	32.60	55.82	65.1
37	Labrador Retriever	Female	5.00	30.50	56.11	65.6
38	Lhasa Apso	Female	10.70	13.20	ND	92.5
39	Lhasa Apso	Female	4.01	7.60	ND	86.2
40	Maltese	Male	6.61	6.00	65.29	80.9
41	Maltese	Male	10.02	3.00	65.29	83.6
42	Maltese	Male	5.52	6.55	65.29	76.9
43	Maltese	Male	6.01	8.90	65.29	88.2
44	Maltese	Female	6.00	2.00	68.83	91.6
45	Maltese	Female	4.94	3.40	68.83	84.7
46	Miniature Schnauzer	Male	9.41	12.80	51.79	77.4
47	Miniature Schnauzer	Female	6.26	5.02	54.99	80.5
48	Old English Sheepdog	Male	3.67	33.10	54.39	68.6
49	Pitbull	Male	2.06	27.10	69.96	72.3
50	Siberian Husky	Female	3.00	18.10	55.17	66.5
51	Silky Terrier	Male	3.00	4.40	58.23	84.5
52	Springer Spaniel	Female	1.13	18.40	49.34	75.3
53	Standard Poodle	Female	7.85	22.60	ND	73.0
54	Weimaraner	Male	3.34	48.40	49.05	66.3
55	Welsh Corgi	Male	5.59	15.10	63.09	72.0
56	West Highland White Terrier	Male	5.90	11.00	60.84	77.9
57	Wheaton Terrier	Male	7.04	19.20	ND	70.6
58	Whippet	Female	15.52	13.60	50.6	72.4
59	Yorkshire Terrier	Female	3.84	3.85	ND	81.9
60	Yorkshire Terrier	Male	13.04	4.20	ND	0.812
61	Yorkshire Terrier	Male	0.75	3.50	ND	79.3

62	Yorkshire Terrier	Male	11.51	3.20	ND	82.5
63	Mixed	Male	5.45	10.50	ND	77.7
64	Mixed	Male	3.67	33.10	ND	68.4
65	Mixed	Male	12.66	34.90	ND	72.0
66	Mixed	Male	10.38	26.50	ND	70.1
67	Mixed	Male	10.55	6.50	ND	78.9
68	Mixed	Female	13.01	24.20	ND	69.5
69	Mixed	Female	6.92	13.40	ND	72.6
70	Mixed	Male	6.02	24.20	ND	71.8
71	Mixed	Male	2.52	39.80	ND	66.9
72	Mixed	Female	2.22	12.00	ND	72.2
73	Mixed	Female	4.71	26.10	ND	62.7
74	Mixed	Male	11.03	16.00	ND	69.4
75	Mixed	Female	6.08	0.00	ND	86.1
76	Mixed	Female	10.24	17.60	ND	76.1
77	Mixed	Male	3.69	20.10	ND	72.1
78	Unknown	ND	ND	ND	ND	82.5
79	Unknown	ND	ND	ND	ND	96.7

Table 1. Subjects in the dataset. Note: Cephalic indices are sex- and breed-specific averages from Stone et al. (2016). Abbreviation: ND, no data.

2.3.2 Image Acquisition and Preprocessing

A 3.0T GE HDx MRI unit with a GE 514,137-2 3.0 HD T/R Quad Extremity Coil was used to acquire transverse and sagittal images. The resolution of the transverse-acquired images ranged from0.234 mm 2 in-plane resolution and 2.699 mm slice distance to0.352 mm 2 in-plane resolution and 3.499 mm slice distance. The resolution of the sagittal-acquired images ranged from 0.273 mm 2in-plane resolution and 3/200 mm slice distance to 0.430 mm 2 in-plane resolution and 3.200 mm slice distance. We combined the transverse and sagittal images by first manually skull-stripping the transverse image,

after which we determined the smallest region of interest (ROI) that fully encompassed the brain from the brain mask image. Next, the transverse image and transverse brain mask were cropped using the ROI coordinates. We then resampled the transverse images to produce isotropic voxels in all three dimensions. The following step involved re-slicing the sagittal image so that it was in the same orientation of the transverse images and then computing a rigid registration from the sagittal image to the original transverse image. After this we cropped the region containing the brain in the sagittal image and registered it to the isotropically resampled transverse brain using a rigid registration. We then rescaled the cropped transverse and sagittal images to ensure that the robust mean of intensity of both images was 100. Lastly, we averaged the images together and applied the brain mask to this combined image.

2.3.3 Template Creation

We registered images to a study-specific template using ANTS (Avants, Tustison, and Song 2009), corrected bias fields using the Atropos N4 tool (Avants et al. 2011), and used the FSL FASTtool to segment gray matter, white matter, and cerebrospinal fluid (Zhang, Brady, and Smith 2001).

2.3.4 Neurocephalic Index Calculation

To generate the neurocephalic index for each subject, the maximally distant points on the left–right, rostral–caudal, and dorsal–ventral axes were measured manually by an undergraduate student research assistant who identified the voxel at the most maximally distant points and used Euclidian geometry to compute distances (see Figure 1). These measurements were then used to calculate the ratio of brain width to brain length × 100. The neurocephalic measurements are identical to the ones used in Hecht et al. (2019). Neurocephalic index was implemented as a continuous variable in our subsequent analysis.

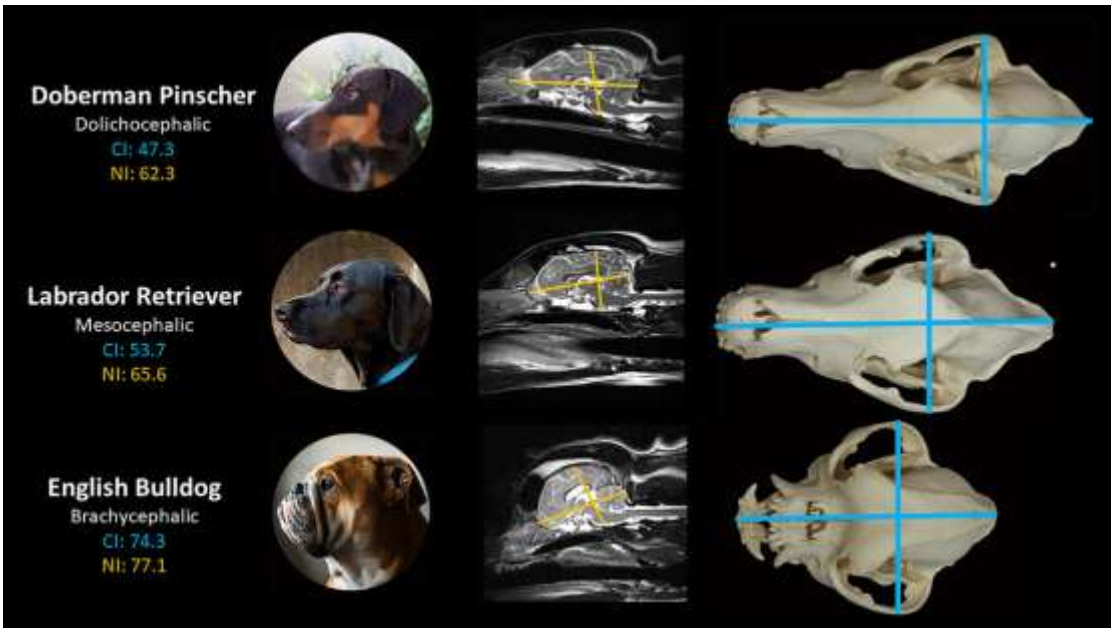

Figure 1. Cephalic index (CI) and neurocephalic index (NI) for three breeds—Doberman pinscher, Labrador retriever, and English bulldog. Yellow lines overlaying sagittal brain images demonstrate brain width and brain length measurements collected to compute NI. Purple lines overlaying skull images demonstrate skull length and width measurement used to generate breed CI average from Stone et al. (2016) dataset. *Source:* Skull images from https://skullbase.info.

2.3.5 Statistical Analyses

In the present analysis, we performed voxel-based morphometry, which measures how brain anatomy varies across individuals in the dataset by assessing where and how much each subject's brain image has to deform in order to align with the group average Jacobian determinant images were produced using nonlinear registration via the ANTS software package (Avants, Tustison, and Song 2009). These Jacobian images are essentially "heat maps" of the spatial transformation that had to occur to align each dog's brain with the group average. In order to restrict analysis to gray matter voxels, each subject's Jacobian image was multiplied by their gray matter mask. The resultant images were used to drive a whole-brain, data-driven voxel-based morphometry analysis by applying voxelwise permutation testing of a general linear model incorporating neurocephalic index using FSL's randomize tool (Winkler et al.

2014). The statistical threshold was set to at p < 0.05using threshold-free cluster enhancement (TFCE) for familywise error correction (Smith and Nichols 2009).

2.4 Results

When examining the continuous relationship between neurocephalic index and gray matter morphology, we found that the higher a dog's neurocephalic index (shorter, wider neurocranium), the lower the gray matter volume in parts of the composite gyrus, suprasylvian gyrus, postcruciate gyrus, right olfactory bulb, ectomarginal gyrus, and cerebellum (see Figure 2, Table 2). On the other hand, the lower a dog's neurocephalic index (narrower, longer crania), gray matter volume was reduced in parts of the olfactory bulb, prorean gyrus, precruciate gyrus, postcruciate gyrus, sylvian gyrus, ectosylvian gyrus, suprasylvian gyrus, composite gyrus, ectomarginal gyrus, cingulate gyrus, piriform lobe, amygdala, hypothalamus, hippocampus, periaqueductal gray, cerebellum, and brainstem (see Figure 3, Table 3). Increased neurocephalic index and decreased neurocephalic index were both associated exclusively with volume reductions, rather than volume expansions. In other words, compared to dogs with mid-range neurocephalic indices (mesocephalic dogs), dogs with both high and low neurocephalic indices (brachycephalic and dolichocephalic dogs) have reduced gray matter in different regions (Figure 4–7).

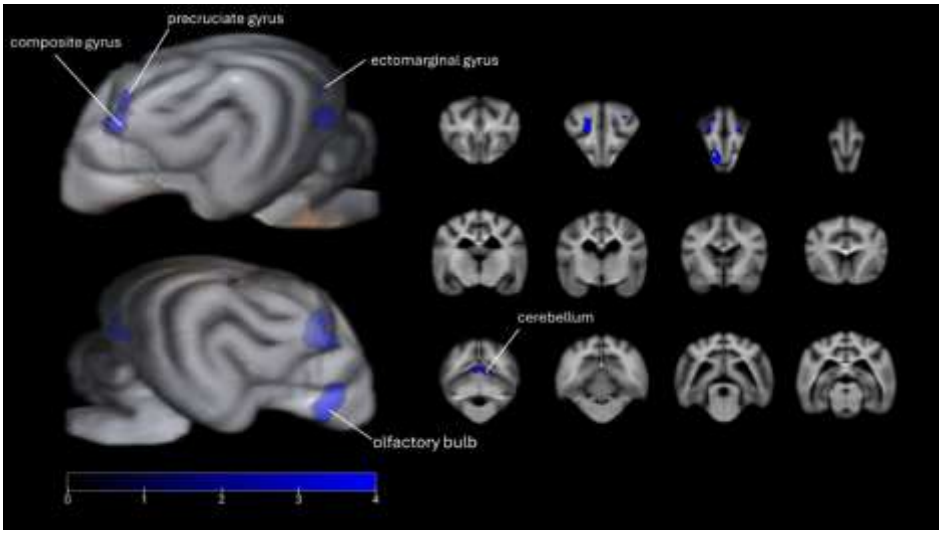

Figure 2. Significantly smaller regions of gray matter volume in brachycephalic dogs resulting from whole-brain voxel-based morphometry analysis. Colored regions are $p < 0.05$ after correction for multiple comparisons; *t*-statistic values are illustrated.

Cluster index	Voxels	T Max	Max *X*	Max *Y*	Max *Z*	COG *X*	COG *Y*	COG *Z*
6	1338	6.13	107	74	141	108	73.7	147
6		5.82	104	75	142			
6		5.51	106	73	154			
6		4.19	114	77	155			
6		4.16	117	76	155			
5	871	6.68	113	75	108	118	76.6	106
5		6.15	118	75	108			
5		4.97	118	74	95			
4	722	4.96	137	22	143	131	23.4	145
4		4.5	130	22	149			
4		4.33	121	25	145			
4		4.12	122	22	149			
4		3.97	120	22	150			
3	650	6.7	151	75	141	150	74.1	147
3		5.66	157	74	155			
3		4.68	141	72	148			
2	66	4.51	119	23	156	119	22.7	155
1	54	5.51	134	24	162	133	23.6	162

Table 2. Cluster information for t-statistic 1 (extreme brachycephaly) depicted in Figure 2. Note: The first line of each cluster shows the global peak and overall center of gravity (COG). The lines of this table show the locations of additional local maxima.

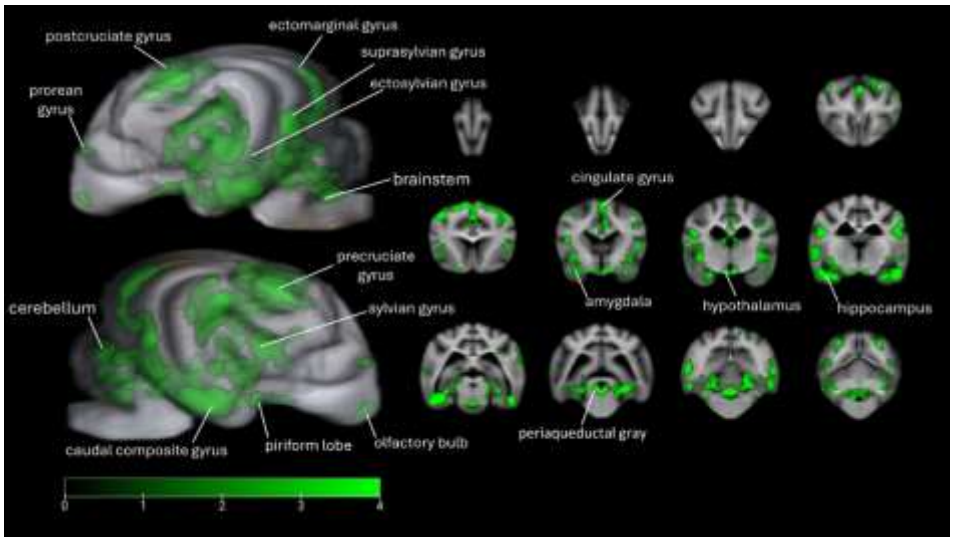

Figure 3. Significantly smaller regions of gray matter volume in dolichocephalic dogs resulting from whole-brain voxel-based morphometry analysis. Colored regions are $p < 0.05$ after correction for multiple comparisons; *t*-statistic values are illustrated.

Cluster index	Voxels	T Max	Max *X*	Max *Y*	Max *Z*	COG *X*	COG *Y*	COG *Z*
7	52,529	7.55	130	25	109	128	43.2	129
7		7.3	136	32	113			
7		6.77	172	41	103			
7		6.71	82	44	100			
7		6.5	102	33	114			
7		6.43	127	34	116			
6	1239	5.84	165	59	170	164	60.8	169

6		3.85	164	66	167			
6		2.37	158	65	176			
5	261	6.47	123	84	95	127	84.4	98.1
5		6.28	125	85	97			
5		5.92	130	85	97			
5		5.68	123	82	92			
5		5.36	131	84	95			
4	62	6.41	115	85	125	116	84.4	126
3	54	6.1	140	83	127	140	83.9	128
3		5.98	140	85	128			
2	7	2.71	83	39	156	83.1	38.4	155
1	2	3.88	107	53	174	107	53	174

Table 3. Cluster information for t-statistic 2 (extreme dolichocephaly) depicted in Figure 3. Note: The first line of each cluster shows the global peak and overall center of gravity (COG). The lines of this table show the locations of additional local maxima.

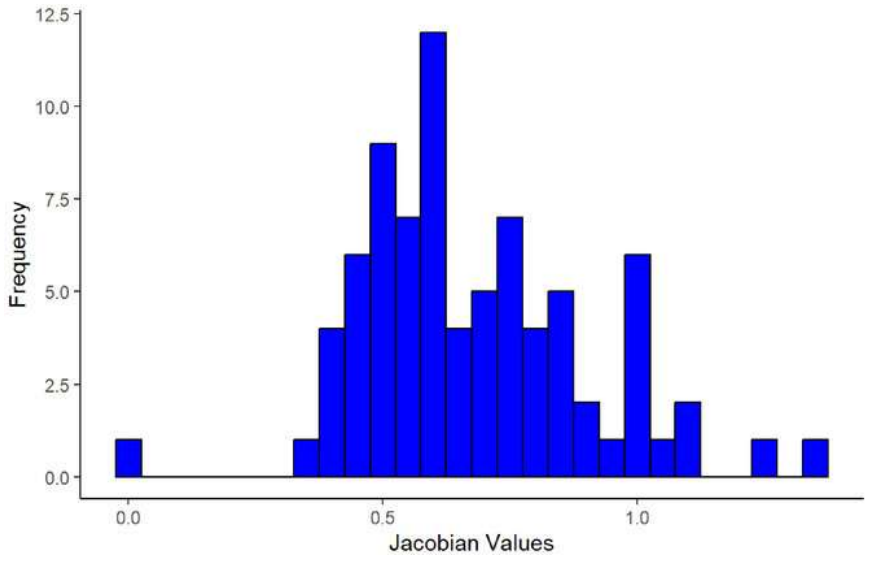

Figure 4. Histogram of Jacobian values representing the degree of expansion necessary for significant regions in Figure 2 to reach the study-specific average volume in dogs with more brachycephalic head shapes.

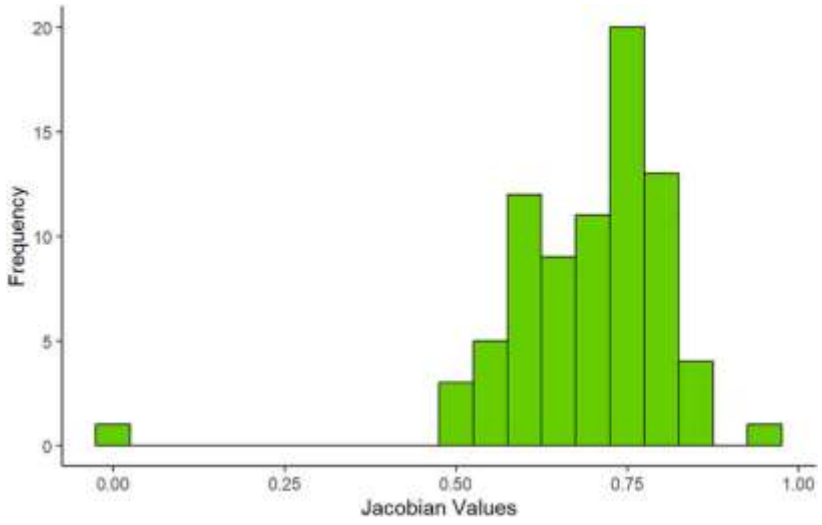

Figure 5. Histogram of Jacobian values representing the degree of expansion necessary for significant regions in Figure 3 to reach the study-specific average volume in dogs with more dolichocephalic head shapes.

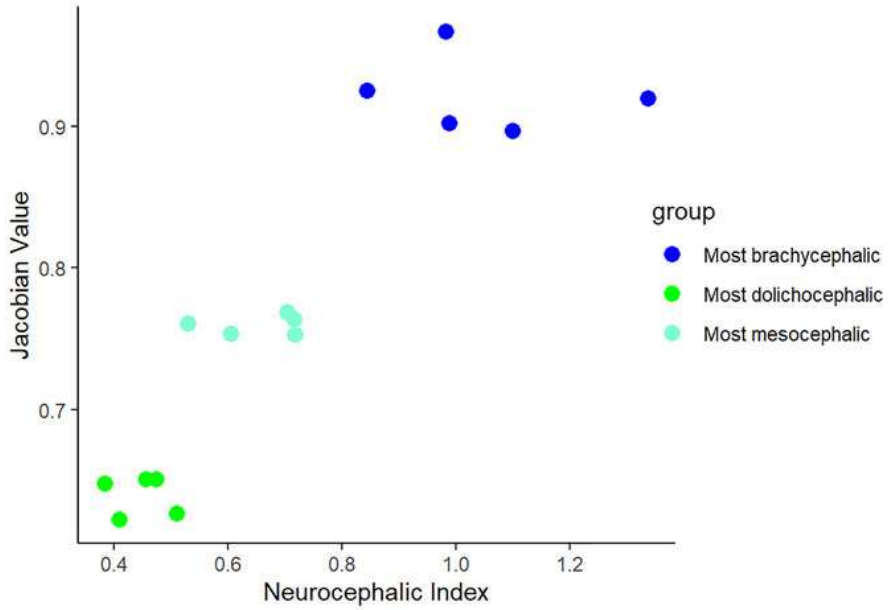

Figure 6. Relationship between neurocephalic index and Jacobian values for the five most brachycephalic, dolichocephalic, and mesocephalic subjects in the dataset for t-statistic 1 (represented in Figure 2).

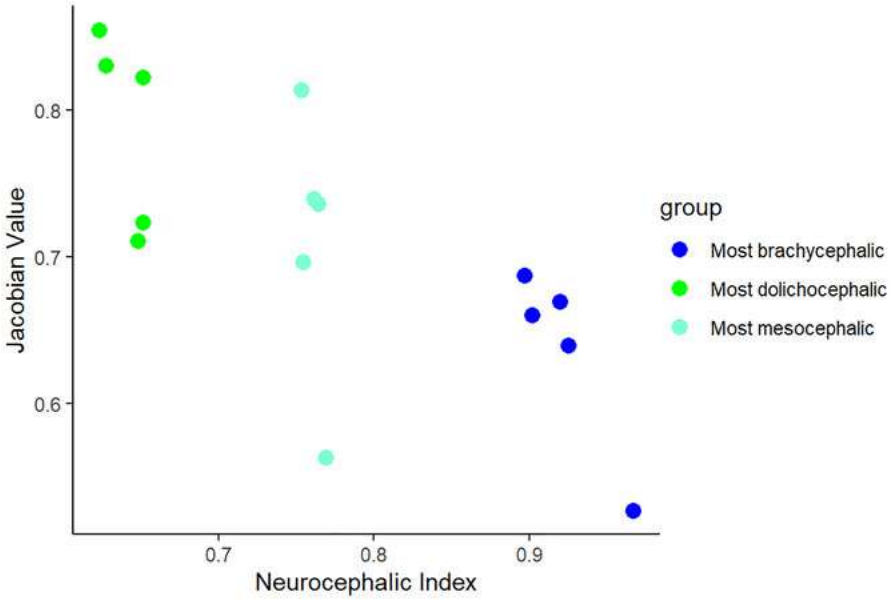

Figure 7. Relationship between neurocephalic index and Jacobian values for the five most brachycephalic, dolichocephalic, and mesocephalic subjects in the dataset for t-statistic 2 (represented in Figure 3).

2.5 Discussion

Domestic dogs show a wide range of variation in head shape, ranging from extreme brachycephaly on one end to extreme dolichocephaly on the other. Brachycephalic dogs have shorter and wider skulls and neurocrania, whereas dolichocephalic dogs have longer and narrower skulls and neurocrania. In this study, we examined variation in head shape by using neurocephalic index as a continuous variable, rather than assigning dogs to predefined head shape categories. We conducted a voxel-based morphometry analysis incorporating MRI studies from 79 dogs. We found that neurocephalic index is associated with significant reductions in several brain regions in dogs with more brachycephalic- and dolichocephalic-shaped heads.

In dogs with more brachycephalic-shaped skulls and higher neurocephalic indices, the regional gray matter volume reductions were restricted to the most rostral and caudal portions of the brain. This is unsurprising given that the neurocranium and skull length are shortened in length in brachycephalic dogs, potentially leaving less space for brain tissue rostrally and caudally. Interestingly, one of the significantly smaller regions was the right olfactory bulb, supporting our hypothesis that the olfactory bulb would be reduced in dogs with more brachycephalic-shaped heads. Previous research has suggested that brachycephalic dogs are poorer at scent detection tasks than other dogs (Polgár et al.2016; Ferrando and Dahl 2022; but see Hall et al. 2015). This could be related to the reduced volume of the right olfactory bulb, which contributes to odor filtering and discrimination (Jia et al. 2014). The directional asymmetry of this finding is striking; the canine neurocranium may exhibit directional asymmetry as well.

Dogs with more brachycephalic-shaped skulls also showed reductions in the volume of the composite gyrus. The composite gyrus includes the secondary somatosensory area (Evans and de Lahunta 2013) and is part of the putative canine default mode network (Szabó et al. 2019). The reductions in this region may be related to altered somatosensory processing and/or cognition, although more research is needed to investigate this possibility.

At the caudal end of the brain, dogs with more brachycephalic-shaped skulls showed reductions in regional gray matter volume within the cerebellum and ectomarginal gyrus. Specifically, within the cerebellum, reduced gray matter volume was observed in the rostral lobe, which is involved in

sensorimotor functions in primates (Schmahmann 2019). Although this hints that brachycephalic dogs may have altered sensorimotor functioning, this has not yet been investigated. Meanwhile, the ectomarginal gyrus is implicated in the visual processing of animate faces and bodies in dogs (Boch et al. 2023), which could suggest differences in social cognition.

Dogs with lower neurocephalic indices, and therefore more dolichocephalic-shaped skulls, showed widely dispersed regional gray matter volume reductions. One of these regions was the anterior portion of the olfactory bulb. Although we also found reductions in the right olfactory bulb in dogs with more brachycephalic-shaped heads, this was in a more posterior region. There is evidence in mice that the anterior and posterior portions of the olfactory bulbs have different functions (Midroit et al. 2021), which could suggest that the reductions of the olfactory bulb at the two head shape extremes may have different functional consequences.

Many regional reductions were observed on the lateral sides of the temporal lobes, which are likely impacted by the narrowing of the width of the cranial cavity. Given the involvement of the temporal lobe in auditory processing (Lipman 1949), a reduction in the volume of the lateral aspect of the temporal lobe may be linked in some manner to previous evidence that dolichocephalic dogs are more reactive to sudden metallic noises, although future research is needed to explore this potential relationship (Stone et al. 2016).Assessment of differential temporal responses to auditory stimuli in dogs of varying head shapes could potentially be a fruitful avenue for future research using functional neuroimaging in awake dogs (Andics et al. 2014; Prichard et al. 2018).

Reductions in regional gray matter volume were also observed in dorsal, rostral, and posterior cerebral cortical brain regions. This may be because the dolichocephalic cranial cavity is not only narrower, but also smaller overall (Brassard et al. 2020).The reduction of the precruciate gyrus, which is premotor cortex(Markow-Rajkowska and Kosmal 1987), and the postcruciate gyrus, which is motor cortex (Evans and de Lahunta 2013), could contribute to altered motor function. The prorean gyrus was also reduced in dogs with more dolichocephalic heads. This may have implications for social cognition, as the size of the prorean gyrus has been hypothesized to relate to pack sociality in canids(Radinsky 1969). Meanwhile, the ectomarginal gyrus has been described as a sensory association cortex (Szabó et al.

2019) and is active when dogs view faces (Boch et al. 2023) and social interactions (Karl et al. 2021). The reduction of this structure in dogs with more dolichocephalic-shaped heads may correspond to altered visual perception of social scenes. This is supported by previous findings that dolichocephalic dogs gaze for shorter periods of time at faces (Bognár, Iotchev, and Kubinyi 2018) and follow pointing gestures less accurately (Gácsi et al. 2009).

Interestingly, several limbic regions implicated in fear, stress, and anxiety, including the amygdala, hypothalamus, and hippocampus (Tovote, Fadok, and Lüthi 2015), are reduced in dogs with more dolichocephalic-shaped skulls. This aligns well with research that has found that dolichocephalic dogs exhibit more social and nonsocial fear than mesocephalic and brachycephalic dogs (McGreevy et al. 2013; Stone et al. 2016). The midbrain, including the periaqueductal gray, was also smaller in dogs with smaller neurocephalic indices, potentially contributing to heightened fear behavior in dolichocephalic dogs (Watson et al. 2016).

As with dogs with more brachycephalic skulls, dogs with more dolichocephalic skulls exhibited regional reductions in the gray matter of the cerebellum. However, in dolichocephalic dogs, these reductions were concentrated in the caudal lobe. The caudal lobe is implicated in both cognitive and emotional functions in primates (Schmahmann 2019). Future studies should investigate if and how cognition and emotion vary across the spectrum of canine head shapes. Lastly, the gray matter volume of the brainstem was also reduced in volume in dolichocephalic dogs.

Altogether, our results show that there is considerable covariation between skull shape and brain anatomy, which may have functional consequences. However, it is unclear whether selection on the skull shape or selection on behavior is the source of regional reductions in brain volume in dogs with extreme head shapes. On the one hand, humans could be selecting for extreme head shapes, and brain/behavior variation may be an unintended side effect (see Figure 8). This is likely the case for dogs bred from conformation/show lines. On the other hand, it is possible that humans could be selecting for behavior variation, and skull variation happens to be a large-effect way for evolution to accomplish this. This may be a plausible evolutionary scenario for dogs bred from working lines. These two possibilities are not necessarily mutually exclusive and may happen simultaneously.

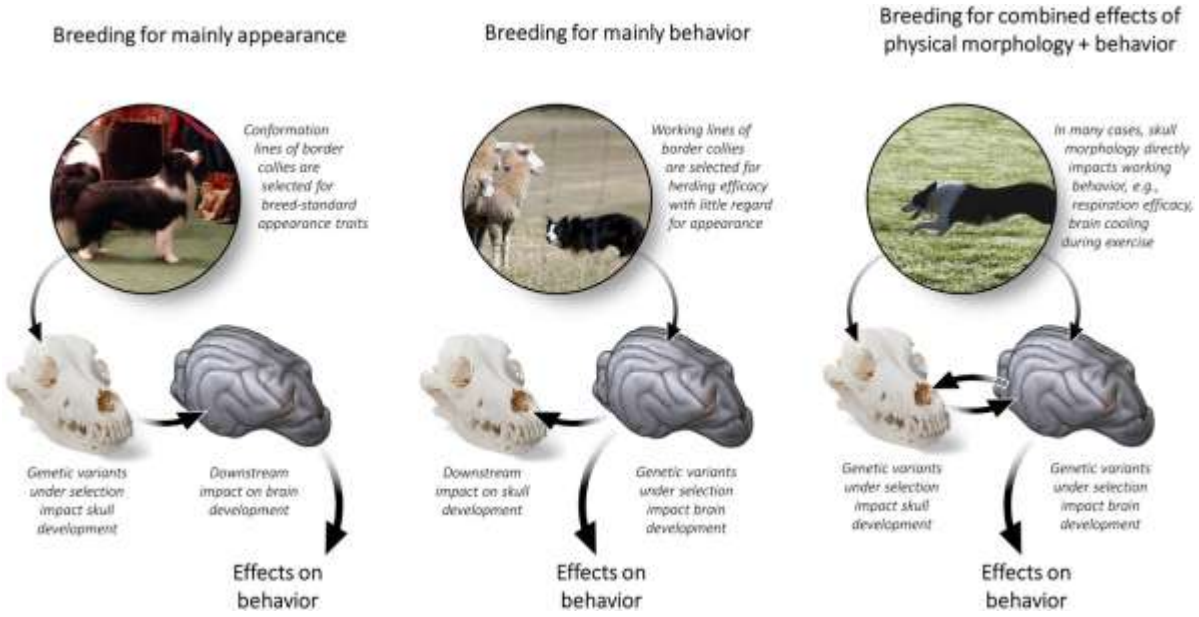

Figure 8. Illustration of potential evolutionary scenarios for skull-brain covariation.

One limitation of our study is that we used neurocephalic index, which represents internal neurocranial dimensions, rather than the more traditionally used cephalic index, which represents external skull dimensions. Although neurocephalic and cephalic indices are positively correlated (Hecht et al. 2019), they do not always have a 1:1 correspondence. Thus, our findings may not be directly comparable with the findings of other studies that used cephalic index.

In this study, we were unable to explore the developmental origins of skull–brain covariation in dogs. Given that brachycephalic skull proportions are already discernable at birth (Andreis et al.2018; Starck 1962), in brachycephalic dogs, it is likely that the brain and skull begin to influence one another's shape during prenatal development. However, this bidirectional influence likely continues until the cranium growth centers close around 12 months of age (Ellenberger and Baum 1977; Ussow 1901). Further research his needed to describe the ontogeny of skull–brain development.

It is important to note that our findings are not directly relevant to understanding skull–brain variation in humans. The dogs we studied are from dog breed populations, which have a fundamentally different structure to human populations (Norton et al.2019). Yet historically, the study of variation in skull shape was used to infer variation in brain structure for nefarious purposes, such as scientific racism in

physical anthropology (Dewbury2007). The field of comparative phrenology, which used skull shape to extrapolate the neurocognitive traits of animals (Combe1843), has been similarly refuted.

However, our results are relevant to understanding how selection pressures that drive variation in skull shape may interact with selection pressures that drive selection on neuroanatomical variation. This may be relevant to our understanding of hominin evolution. For example, shifts in diet drove shifts in jaw and skull structure in early hominins (Strait et al. 2009). Our results suggest that such changes could have also been accompanied by alterations to brain anatomy, which may have been linked with changes in cognition and behavior. Similarly, shifts in skull anatomy during early dog domestication, such as the shortening and widening of the skull (Galeta et al. 2021), could have been associated with shifts in brain organization and therefore cognitive and behavioral traits.

All in all, the present study provides firm evidence that variation in skull shape is directly related to variation in regional gray matter volume in domestic dogs. Our findings add to the existing literature regarding skull–brain covariation in dogs (Czeibertet al. 2020; Doiche et al. 2022; Pilegaard et al. 2017; Selba et al.2020) and solidify dogs as an excellent model organism for studying questions of how the skull and brain relate to one another. Future research should explore whether it is selection on skull shape and/or selection on brain–behavioral phenotypes that is driving covariation in these structures. It would also be fruitful to investigate whether the skull–brain covariation observed in this study has consequences for brain function and behavioral phenotypes in dogs. This is especially pertinent to ongoing discussions of welfare in dogs with extreme head shapes (Ekenstedt, Crosse, and Risselada 2020).

Chapter 3 Neuroanatomical asymmetry in the canine brain

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3.1 Abstract

The brains of humans and non-human primates exhibit left/right asymmetries in grey matter morphology, white matter connections, and functional responses. These asymmetries have been implicated in specialized behavioral adaptations such as language, tool use, and handedness. Left/right asymmetries are also observed in behavioral tendencies across the animal kingdom, suggesting a deep evolutionary origin for the neural mechanisms underlying lateralized behavior. However, it is still unclear to what extent brain asymmetries supporting lateralized behaviors are present in other large-brained animals outside the primate order. Canids and other carnivorans evolved large, complex brains independently and convergently with primates, and exhibit lateralized behaviors. Therefore, domestic dogs offer an opportunity to address this question. We examined T2-weighted MRI images of 62 dogs from 33 breeds, opportunistically collected from a veterinary MRI scanner from dogs who were referred for neurological examination but were not found to show any neuropathology. Volumetrically asymmetric regions of gray matter included portions of the temporal and frontal cortex, in addition to portions of the cerebellum, brainstem, and other subcortical regions. These results are consistent with the perspective that asymmetry may be a common feature underlying the evolution of complex brains and behavior across clades, and provide neuro-organizational information that is likely relevant to the growing field of canine behavioral neuroscience.

3.2 Introduction

Brain asymmetry was long thought to be a uniquely human trait (Kellogg 1898; Sherrington 1922; Rasdolsky 1927). However, it is now recognized that lateralized perceptuomotor behaviors and brain asymmetries occur in a broad range of vertebrate and invertebrate taxa (see Güntürkün et al. 2020 for a

review). For example, chimpanzees, rhesus macaques, olive baboons, vervet monkeys, and tufted capuchins show many regional cortical asymmetries paralleling humans (e.g., Becker et al. 2022; Xia et al. 2021; Xiang et al. 2020; Lopez-Persem et al. 2020; Xia et al. 2019; Marie et al. 2017; Gómez-Robles et al. 2016; Fears et al. 2011; Phillips and Sherwood 2005). This suggests that brain asymmetries are common across the primate order and may relate to primate-specialized functions like communication and tool use (Becker and Meguerditchian 2022). However, the widespread nature of brain asymmetry across phylogeny suggests that it has a deep evolutionary origin and is perhaps a common feature of all nervous systems (Brown and Magat 2011). This may point toward more generalized, non-primate-specific adaptive functions, potentially including parallel processing (Rogers 2000), reduced redundancy and increased processing capacity (Hopkins and Cantolupo 2008), or reduced need for interhemispheric communication through increased specialization (Philips et al. 2015). Additionally, it remains unclear whether the more robust and widespread asymmetries of the human brain are derived adaptations for human-specific cognition and behavior or if they are simply byproducts resulting from our species' evolution of a larger brain (Hopkins et al. 2015).

Domestic dogs provide an ideal opportunity to examine these questions. Through adaptive radiation caused by artificial human selection, dogs have assumed many different morphological and behavioral traits specialized for various human-constructed niches. Like language and tool use, many of these behaviors are heavily dependent on learning and training (Coppinger and Coppinger 2002). Breeds of dogs also show large intraspecific variations in both body size (Sutter et al. 2008) and brain size (Hecht et al. 2019). If asymmetry emerges from brain scaling, it should be apparent across dog breeds.

Specialized working behaviors show evidence of lateralization in dogs. For example, protection and herding dogs show a left visual hemifield, and right hemisphere bias when exhibiting aggressive behaviors towards their respective targets–livestock or a person wearing a bite sleeve (Siniscalchi et al. 2013, 2019), and laterality tests are a significant predictor of success in guide dogs and racing greyhounds (Tomkins et al. 2012; Schneider et al. 2012). More generally, at a species level, dogs exhibit lateralized preferences in paw usage (Ocklenburg et al. 2019), nostril usage (Siniscalchi et al. 2016),

facial expressions (Nagasawa et al. 2013) head-turning (Siniscalchi et al. 2010), and tail wagging (Gobbo and Šemrov 2021) (see Siniscalchi et al. 2017 for a review).

However, despite a few limited analyses (Tan and Çalşikan 1987; Koyun et al. 2011; Rağbetli et al. 2010), asymmetry in the canine brain has yet to be thoroughly investigated. Recently, a growing number of functional MRI studies point toward functional lateralization, including in sensory regions (Andics et al. 2014; Gábor et al. 2020; Jia et al. 2014), higher-order cognitive regions (Cook et al. 2016), and some brain networks (Szabó et al. 2019). Yet very little is known about the regional structural asymmetries that may underlie these functional asymmetries (Datta et al. 2012).

To address these gaps, we investigated gray matter asymmetries in a previously published MRI dataset of 62 purebred dogs of 33 different breeds (Hecht et al. 2019). We hypothesized that (1) dog brains would show asymmetries in whole hemisphere and regional gray matter volume, (2) structural brain networks discovered by Hecht et al. (2019) would show asymmetries in grey matter volume, and (3) the volume of gray matter asymmetries would vary with brain size, age, and sex, based on previous findings in humans (Kong et al. 2018), as well as breed group, since it is associated with brain organization in dogs (Hecht et al. 2019).

3.3 Methods

3.3.1 Subjects

A previously published dataset (Hecht et al. 2019) which included T2-weighted MRI scans from 62 purebred dogs of 33 different breeds was used in this study. This dataset was opportunistically acquired from the Veterinary Teaching Hospital at the University of Georgia at Athens. All scans were from dogs who were diagnosed with no observable structural brain abnormalities by a veterinary neurologist (M.K.). Information about the age, sex, breed, body mass, and brain volume of each dog included in this dataset are shown in Table 4.

ID	Breed	Sex	Age	Body mass (kg)	Cephalic index (from database)	Neurocephalic index
1	Basset Hound	Male	4.02	28.10	51.89	74.1
2	Beagle	Male	14.29	17.00	61.82	73.8
3	Beagle	Male	4.04	11.70	61.82	76.4
4	Beagle	Male	ND	28.50	61.82	84.8
5	Beagle	Male	4.00	8.30	61.82	82.4
6	Beagle	Male	1.69	28.50	61.82	77.8
7	Bichon Frise	Male	9.01	9.30	61.51	80.4
8	Border Collie	Male	6.05	28.20	54.38	65.2
9	Border Collie	Male	5.56	20.60	54.38	65.3
10	Boston Terrier	Male	11.90	12.50	92.62	90.2
11	Boston Terrier	Male	5.80	8.90	92.62	89.7
12	Boxer	Male	8.08	31.75	67.19	67.6
13	Boxer	Male	5.01	34.20	67.19	67.3
14	Boxer	Female	10.72	31.75	66.28	83.2
15	Boxer	Male	9.25	40.80	67.19	69.7
16	Bulldog	Male	1.00	16.78	90.18	74.0
17	Bulldog	Male	4.42	30.00	90.18	77.1
18	Cavalier King Charles Spaniel	Female	0.47	3.20	76.77	81.4
19	Cavalier King Charles Spaniel	Female	0.47	14.50	76.77	92.0
20	Cocker Spaniel	Female	6.38	18.10	61.01	75.4
21	Dachshund	Female	11.30	4.90	51.76	79.2
22	Dachshund	Female	6.56	6.40	51.76	77.3
23	Dachshund	Male	7.83	5.60	49.59	81.2
24	Dachshund	Female	1.81	5.30	51.76	81.1
25	Doberman Pinscher	Female	4.67	29.80	46.96	62.3

26	English Pointer	Male	7.34	27.30	ND	74.2
27	German Shorthaired Pointer	Female	6.17	27.00	48.3	73.4
28	Golden Retriever	Male	10.01	39.80	56.52	68.9
29	Golden Retriever	Male	6.01	42.20	56.52	70.1
30	Golden Retriever	Male	11.01	34.90	56.52	68.0
31	Greyhound	Female	7.52	36.70	45.83	64.8
32	Greyhound	Male	3.82	37.10	46.84	65.1
33	Greyhound	Female	2.20	36.00	45.83	66.5
34	Jack Russell Terrier	Male	ND	14.00	59.28	80.1
35	Keeshond	Male	7.17	21.60	60.18	71.0
36	Labrador Retriever	Male	9.72	32.60	55.82	65.1
37	Labrador Retriever	Female	5.00	30.50	56.11	65.6
38	Lhasa Apso	Female	10.70	13.20	ND	92.5
39	Lhasa Apso	Female	4.01	7.60	ND	86.2
40	Maltese	Male	6.61	6.00	65.29	80.9
41	Maltese	Male	10.02	3.00	65.29	83.6
42	Maltese	Male	5.52	6.55	65.29	76.9
43	Maltese	Male	6.01	8.90	65.29	88.2
44	Maltese	Female	6.00	2.00	68.83	91.6
45	Maltese	Female	4.94	3.40	68.83	84.7
46	Miniature Schnauzer	Male	9.41	12.80	51.79	77.4
47	Miniature Schnauzer	Female	6.26	5.02	54.99	80.5
48	Old English Sheepdog	Male	3.67	33.10	54.39	68.6
49	Pitbull	Male	2.06	27.10	69.96	72.3
50	Siberian Husky	Female	3.00	18.10	55.17	66.5
51	Silky Terrier	Male	3.00	4.40	58.23	84.5
52	Springer Spaniel	Female	1.13	18.40	49.34	75.3

53	Standard Poodle	Female	7.85	22.60	ND	73.0
54	Weimaraner	Male	3.34	48.40	49.05	66.3
55	Welsh Corgi	Male	5.59	15.10	63.09	72.0
56	West Highland White Terrier	Male	5.90	11.00	60.84	77.9
57	Wheaton Terrier	Male	7.04	19.20	ND	70.6
58	Whippet	Female	15.52	13.60	50.6	72.4
59	Yorkshire Terrier	Female	3.84	3.85	ND	81.9
60	Yorkshire Terrier	Male	13.04	4.20	ND	0.812
61	Yorkshire Terrier	Male	0.75	3.50	ND	79.3
62	Yorkshire Terrier	Male	11.51	3.20	ND	82.5

Table 4. Subjects included in analysis. ND means no data.

3.3.2 Image Acquisition and Preprocessing

Images in this dataset were collected using a 3.0T GE HDx MRI unit with a GE 514,137-2 3.0 HD T/R Quad Extremity Coil. The same image preprocessing pipeline was used in this study as was conducted in Hecht et al. (2019) and Hecht et al. (2021). This involved registering images to a study-specific template using ANTS (Avants et al. 2009), correcting bias fields using the Atropos N4 tool (Avants et al. 2011), and segmenting images for grey matter, white matter, and cerebrospinal fluid via the FSL FAST tool (Zhang et al. 2001).

3.3.4 Statistical Analyses

After FAST image segmentation and ANTS registration, each subject's grey matter mask was multiplied by the Jacobian of the ANTS warpfield. This produced a Jacobian image containing only grey matter voxels, representing a "heat map" of the spatial transformation required to align each subject's brain with the group average. These grey matter "heat maps" became the input for two further, complementary analyses.

First, we applied an in-house version of FSL's voxel-based morphometry (VBM) tool (Behrens et al. 2003) that was modified to incorporate ANTS-based nonlinear registration. In this analysis, all subject's

Jacobian-modulated grey matter images were averaged, left–right flipped, and averaged again to create a symmetrical template. Nonlinear registrations were computed between each subject's grey matter segmentation and this symmetrical template. Finally, the resultant grey-matter-masked-Jacobians were subjected to Monte Carlo permutation testing on a general linear model using FSL's randomise tool (Winkler et al. 2014), with threshold-free cluster enhancement for multiple comparisons correction (Smith and Nichols 2009). A one-sample *t* test was used to identify voxels that showed significant volumetric differences between the left and right hemispheres. We next examined the volume of the left and right hemispheres of each dog by warping template-space hemisphere masks to each dog's image and measuring the resultant native-space volume.

Second, we analyzed asymmetries in brain networks resulting from carrying out source-based morphometry (SBM; Gupta et al. 2019; Xu et al. 2009) in the same dataset. SBM is a multivariate alternative to VBM. While VBM inherently relies on a user-specified general linear model, SBM uses independent components analysis to identify regionally covarying gray matter networks in a data-driven way. Each network is composed of anticorrelated components: across subjects, when regions in one component tend to be larger, regions in the other component tend to be smaller, and vice versa. These morphologically covarying structural networks are similar to functionally covarying resting state networks and are thought to reflect the combined effects of genetic factors, developmental trajectories, and functional specialization (Alexander-Bloch et al. 2013; Evans 2013; Gupta et al. 2019). We previously identified 6 such networks in the canine brain (Hecht et al. 2019). Asymmetries in these networks could, therefore, point toward functional lateralization. Therefore, we identified voxels within each component of each network that were present in one hemisphere but not the other.

Finally, subject information (see Table 4) and significant asymmetrical grey matter cluster volumes derived from the VBM analysis were imported into R (R Core Team 2021) to analyze the relationship between the asymmetrical volume of each network with brain volume, age, sex, and breed group using generalized linear models.

3.4 Results

Significant gray matter volume asymmetries were observed in the canine brain via voxel-based morphometry (VBM) (see Figure 9). Regions showing leftward asymmetry included parts of the olfactory peduncle, piriform lobe, precruciate sulcus, prorean gyrus, sylvian gyrus, sylvian sulcus, composite gyrus, ectosylvian gyrus, suprasylvian gyrus, amygdala, cerebellum, and brainstem. Regions showing rightward asymmetry included parts of the olfactory peduncle, prorean gyrus, precruciate gyrus, postcruciate gyrus, coronal gyrus, hypothalamus, thalamus, cerebellum, and brainstem.

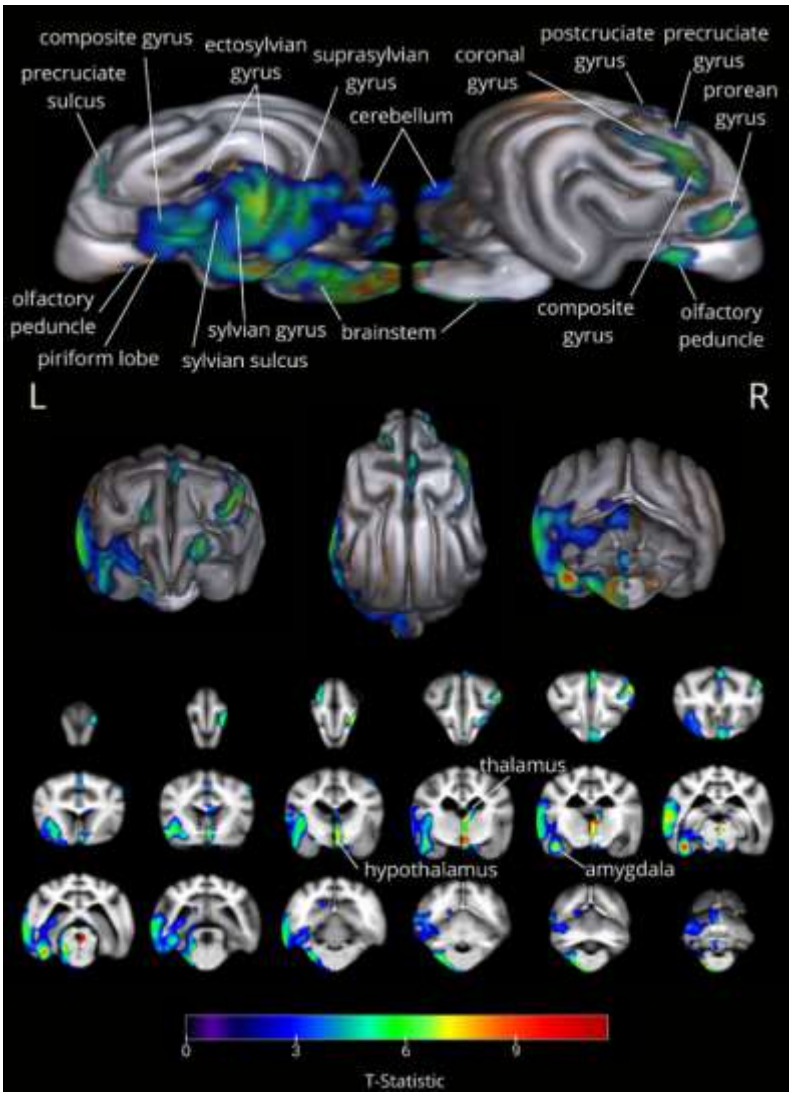

Figure 9. Asymmetrical regions of gray matter volume in domestic dogs resulting from whole-brain voxel-based morphometry analysis. Colored regions are all $p < 0.05$ after correction for multiple comparisons; *t* statistic values are illustrated.

We generated seven generalized linear models to test whether significantly asymmetrical volumes of gray matter were best predicted by brain volume, age, sex, and/or breed group for each significantly asymmetrical cluster derived from our VBM analysis (see Table 5 and Supplemental Figures 31–35). Only two clusters showed any significant main effects. Cluster 3, which is located in the piriform cortex, showed significant main effects for sex ($t = 2.895$, $p < 0.05$) and the scent-hunting breed group ($t = 2.907$, $p < 0.05$). Cluster 7, which is located in the hippocampus, presented significant main effects for the sight hunting ($t = 2.809$, $p < 0.05$) and vermin control ($t = -2.729$, $p < 0.05$) breed groups.

		Cluster 1	**Cluster 2**	**Cluster 3**	**Cluster 4**	**Cluster 5**	**Cluster 6**	**Cluster 7**
Intercept	*p* value	0.749	0.947	0.247	0.919	0.383	1.000	**0.035***
	Standard Error	0.092	0.108	0.063	0.039	0.045	0.022	0.022
Brain Volume	*p* value	0.749	0.947	0.855	0.919	0.724	1.000	0.685
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	Beta coefficient	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Age	*p* value	0.783	0.947	0.055	0.964	0.141	1.000	0.877
	Standard error	0.003	0.004	0.002	0.001	0.002	0.001	0.001
	Beta coefficient	0.000	0.000	− 0.010	0.000	0.010	0.000	0.000
Sex: Male	*p* value	0.783	0.947	**0.034***	0.919	0.724	1.000	0.877
	Standard error	0.028	0.033	0.019	0.012	0.014	0.007	0.007
	Beta coefficient	0.020	0.000	− 0.060	0.010	0.010	0.000	0.000

Breed Group: Explicit Companionship	*p* value	0.783	0.947	0.855	0.964	0.600	1.000	0.324
	Standard error	0.051	0.060	0.035	0.022	0.025	0.012	0.012
	Beta coefficient	− 0.020	0.040	0.010	0.000	− 0.030	0.000	− 0.020
Breed Group: Guarding	*p* value	0.783	0.947	0.652	0.919	0.831	1.000	0.324
	Standard error	0.042	0.049	0.029	0.018	0.021	0.010	0.010
	Beta coefficient	0.020	0.040	0.020	− 0.010	0.000	0.010	− 0.010
Breed Group: Herding	*p* value	0.783	0.947	0.697	0.919	0.669	1.000	0.685
	Standard error	0.054	0.063	0.037	0.023	0.026	0.013	0.013
	Beta coefficient	0.030	0.000	0.020	− 0.030	− 0.030	0.010	− 0.010
Breed Group: Scent Hunting	*p* value	0.783	0.947	**0.034***	0.919	0.724	1.000	0.592
	Standard error	0.045	0.053	0.031	0.020	0.022	0.011	0.011
	Beta coefficient	− 0.050	0.040	0.090	− 0.010	− 0.020	0.010	− 0.010
Breed Group: Sight Hunting	*p* value	0.749	0.947	0.653	0.919	0.382	1.000	**0.035***
	Standard error	0.049	0.057	0.034	0.021	0.024	0.012	0.011
	Beta coefficient	0.070	0.020	− 0.030	0.010	− 0.040	− 0.010	− 0.030
	p value	0.783	0.947	0.653	0.964	0.831	1.000	0.685

Breed Group: Sledding	Standard error	0.093	0.110	0.064	0.040	0.046	0.023	0.022
	Beta coefficient	0.060	0.140	− 0.050	0.000	− 0.010	0.010	− 0.020
Breed Group: Sport Fighting	*p* value	0.841	0.947	0.855	0.919	0.724	1.000	0.324
	Standard error	0.063	0.074	0.043	0.027	0.031	0.015	0.015
	Beta coefficient	− 0.010	0.060	0.010	0.020	− 0.020	0.010	− 0.020
Breed Group: Vermin Control	*p* value	0.783	0.947	0.472	0.919	0.783	1.000	**0.035***
	Standard error	0.059	0.070	0.041	0.026	0.029	0.015	0.014
	Beta coefficient	− 0.030	− 0.030	0.050	0.010	− 0.010	0.000	− 0.040

Table 5. Summaries of the seven generalized linear mixed models created for each asymmetrical cluster generated by the VBM analysis. *p* values were corrected for multiple comparisons using the Benjamini and Hochberg procedure (Benjamini and Hochberg, 1995). Significant values ($p < 0.05$) are bolded and starred.

We also performed a paired two-tailed *t* test to evaluate potential whole hemisphere differences in gray matter volume. We found that the left hemisphere is significantly larger than the right hemisphere ($t = 13.634$, $p < 0.05$).

Our source-based morphometry (SBM) analysis revealed that several of the previously published structural brain networks (Hecht et al. 2019) show regional asymmetries in gray matter volume (see Figure 10). In network 1, regions that showed leftward asymmetry in gray matter volume included parts of the olfactory peduncle, composite gyrus, ectosylvian gyrus, suprasylvian gyrus, ectomarginal gyrus, hippocampus, and cerebellum (see Supplemental Figure 25). Rightwardly asymmetric regions included parts of the composite gyrus, central sulcus, sylvian gyrus, suprasylvian gyrus, and cerebellum. The

symmetric regions across both hemispheres included the olfactory peduncle, sylvian gyrus, putamen, and caudate nucleus. Network 1 is thought to encapsulate the mesolimbic reward system and may be involved in social behavior (Hecht et al. 2019).

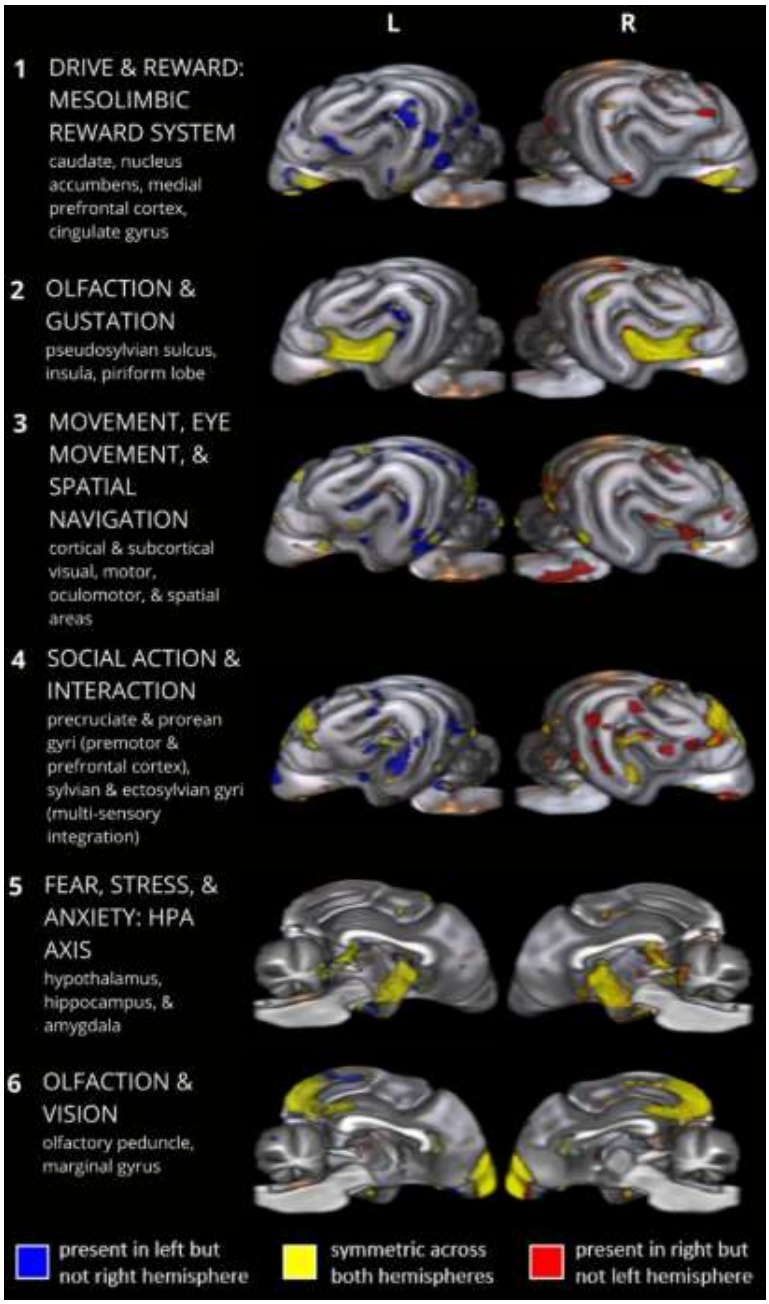

Figure 10. Asymmetrical and symmetrical regions of gray matter volume in six brain networks in domestic dogs, as identified with whole-brain source-based morphometry analysis. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.

Regions of network 2 that demonstrated leftward asymmetries in gray matter volume included parts of the ectosylvian sulcus and caudate nucleus (see Supplemental Figure 26). Rightward asymmetry was observed in the gray matter volume of parts of the marginal gyrus and ectomarginal gyrus. Network 2 regions that were symmetrical across both hemispheres included parts of the olfactory peduncle, olfactory sulcus, presylvian sulcus, sylvian gyrus, sylvian sulcus, ectosylvian gyrus, ectomarginal gyrus, insula, and putamen. Hecht et al. (2019) posited that this network is involved in olfaction and gustation.

Network 3 regions that demonstrated leftward asymmetries in gray matter volume consisted of parts of the ectosylvian sulcus, ectomarginal gyrus, suprasylvian gyrus, and suprasylvian sulcus (see Supplemental Figure 27). Rightwardly asymmetric regions of gray matter volume included parts of the sylvian gyrus, prorean gyrus, precruciate gyrus, ectomarginal gyrus, marginal gyrus, cerebellum, and brainstem. Network 3 regions that were symmetrical across both hemispheres included parts of the olfactory peduncle, frontal gyrus, sylvian gyrus, suprasylvian gyrus, and cerebellum. This network may play a role in movement through space (Hecht et al. 2019).

In network 4, regions with leftward asymmetrical gray matter volumes included parts of the olfactory peduncle, piriform lobe, presylvian gyrus, sylvian gyrus, ectosylvian gyrus, ectomarginal gyrus, suprasylvian gyrus, and brainstem (see Supplemental Figure 28). Rightwardly asymmetric regions of network 4 consisted of parts of the olfactory peduncle, composite gyrus, sylvian gyrus, suprasylvian gyrus, ectosylvian gyrus, ectosylvian sulcus and amgydala. Regions of network 4 that had symmetric areas of gray matter volume across both hemispheres included parts of the presylvian sulcus, frontal gyrus, postcruciate gyrus, cingulate gyrus, marginal gyrus, sylvian gyrus, and cerebellum. Network 4 is thought to be involved in social interaction (Hecht et al. 2019).

Network 5 showed leftward asymmetry in the gray matter volume of parts of the suprasylvian gyrus and parahippocampal gyrus (see Supplemental Figure 29). Network 5 demonstrated rightward asymmetry in the gray matter volume of parts of the suprasylvian gyrus, coronal sulcus, and marginal gyrus. Regions that showed symmetric gray matter volumes across both hemispheres included parts of the hypothalamus, caudate nucleus, and hippocampus. This network involves regions of the HPA axis, and therefore may be involved in responses to environmental threats (Hecht et al. 2019).

In network 6, a part of the marginal gyrus showed asymmetrical gray matter volume in the left hemisphere (see Supplemental Figure 30). Rightward asymmetry occurred in parts of the olfactory peduncle and ectomarginal gyrus. Regions of network 6 that were symmetric across both hemispheres included parts of the olfactory peduncle and marginal gyrus. Network 6 is likely involved in the early processing of olfaction and vision (Hecht et al. 2019).

3.5 Discussion

Dogs have complex, lateralized behaviors and wide variation in brain size, providing an ideal opportunity to assess relationships between brain size, behavioral lateralization, and brain asymmetries. Here, we performed complementary voxel-based and source-based morphometry analyses using MRI images from 62 dogs of 33 breeds. We found widespread canine gray matter asymmetries.

Notably, dogs show leftward asymmetries in temporal cortical regions—particularly in and around the sylvian sulcus, which is the canine analogue of the primate sylvian fissure (Bryant and Preuss 2018). This territory is modified by selection for social behavior in the Russian farm-fox experiment—compared to aggressive foxes, tame foxes show an expansion of the sylvian gyrus and ectosylvian sulcus, whereas compared to tame foxes, aggressive foxes show an expansion of the sylvian sulcus (Hecht et al. 2021). It is associated with dog breeds historically selected for human social companionship (Hecht et al. 2019). There is robust evidence that the human sylvian fissure and perisylvian cortex also show a leftward bias in structural features (Takao et al. 2011; Gómez-Robles et al. 2016; Maingault et al. 2016). These regions have been implicated in language processing (Price 2012), although chimpanzees (Hopkins & Avants 2013; Vickery et al. 2020) and olive baboons (Marie et al. 2017) also show leftward asymmetries here, suggesting that simpler forms of communication and/or other functions may be responsible for the evolution of asymmetry in this region. Canine fMRI studies find that the dog temporal cortex is involved in the visual and auditory perception of humans and other dogs (Cuaya et al. 2016; Andics and Miklosi 2018; Thompkins et al. 2018; Boros et al. 2020; Cuaya et al. 2022), including processing of human speech intonation in the middle ectosylvian gyrus (Andics et al. 2016). However, Andics et al. (2016) found evidence for a right hemispheric bias for processing lexically marked words, while other studies examining auditory processing in the canine temporal lobe have found little evidence for functional

lateralization (Boros et al. 2020; Cuaya et al. 2022). There may be a lack of a 1:1 correspondence between structural asymmetries and functional activity in this region—or alternatively, structural asymmetries in the temporal lobe may relate to lateralized functional activity for something other than auditory processing. Additionally, the human brain shows some rightward temporal lobe asymmetries, including the superior temporal sulcus (Maingault et al. 2016), but we did not observe this pattern in dogs.

We also found that several regions of the dog frontal cortex are rightwardly asymmetric. This includes the prorean gyrus, which is a prefrontal region that connects with distributed neocortical regions, including temporal auditory association regions and parts of the parietal and occipital cortex, as well as medial temporal lobe regions and the mediodorsal thalamic nucleus (Kreiner 1961; Kosmal and Dabrowska 1980; Markow-Rajkowska and Kosmal 1987). The prorean gyrus is implicated in the evolution of complex sociality in carnivorans (Radinsky 1969), historical selection for human companionship in domestic dog breeds (Hecht et al. 2019), and selection on human-directed social behavior in the Russian farm-fox experiment (Hecht et al. 2021). It is likely homologous to primate medial frontal and/or orbitofrontal regions (Preuss and Wise 2022), where human and chimpanzee brains exhibit rightward structural asymmetries (Kong et al. 2018; Vickery et al 2020).

The parietal and occipital lobes of humans and chimpanzees exhibit further asymmetries (Kong et al. 2018; Hopkins et al. 2008), but this is not observed in the canine brain. Thus, although regional asymmetries are present in the dog cortex, they appear to be less spatially distributed.

We also observed subcortical asymmetries in dogs, including leftward asymmetry in the amygdala and rightward asymmetry in the thalamus. In contrast, humans and chimpanzees show rightward amygdala asymmetry (Ocklenburg et al. 2022; Vickery et al. 2020). While chimpanzees also show rightward asymmetry in the thalamus (Vickery et al. 2020), humans appear to have a leftward asymmetry in this structure (Kang et al. 2015).

Cerebellar structural asymmetries were broadly leftward. This included the anterior lobe, HVI lobule, and HVII lobule. This is consistent with earlier work that reported leftward asymmetry in the canine cerebellum as an entire structure (Koyun et al. 2011). Meanwhile, the chimpanzee cerebellum shows rightward GMV asymmetries (Vickery et al. 2020). Because each hemisphere of the cerebellum is

predominantly connected to the contralateral cerebral hemisphere in many species (Buckner 2013; Schmahmann 2016), leftward cerebellar asymmetries might have coevolved with rightward frontal asymmetries in dogs. The anterior lobe contributes to sensorimotor functions (Schmahmann 2019), so the leftward anterior lobe asymmetry may relate to the rightward prefrontal asymmetry noted above.

Finally, we observed widespread leftward asymmetries in the dog brainstem. The brainstem is understudied in MRI research (Elvsåshagen et al. 2020), making it difficult to determine whether the pattern observed here also exists in primates. Interestingly, though, orbitofrontal and medial prefrontal regions, which are rightwardly asymmetric in the current dog dataset and in chimpanzees and humans (Kong et al. 2018; Vickery et al. 2020), project to brainstem autonomic regions via the hypothalamus in rhesus macaque monkeys (Barbas et al. 2003). Additional research is needed to determine whether the canine prefrontal and brainstem asymmetries reported here are related.

Interestingly, the left hemisphere was significantly larger than the right, in contrast to an earlier study using mixed breed dogs which found the opposite result (Tan and Çalşikan 1987). Further research is needed to determine whether breed, sex, age, and/or environment/life history factors could account for this discrepancy.

The presence of asymmetries in all 6 of the networks associated with historical working behaviors (Hecht et al. 2019) suggests that structural asymmetries could have behavioral consequences. For example, network 4 is implicated in social action and interaction and was one of the most asymmetrical networks in our analysis. It is associated with historical specialization for human companionship (i.e., in toy breeds), as well as with police/military and herding working behaviors. Interestingly, biting humans or livestock is a lateralized, aggressive behavior that is more likely to emerge when the target is in the left visual hemifield and is biased towards the right hemisphere for processing (Siniscalchi et al. 2013, 2019). Speculatively, asymmetries in this network might support the lateralization of controlled aggression. Additionally, several voxel-based morphometry clusters were associated with historical working functions. Cluster 3 was significantly linked to scent hunting breed ancestry and was located in the piriform cortex, which has olfactory functions and is also implicated in scent hunting ancestry in our earlier source-based morphometry analysis (Hecht et al. 2019). Cluster 7, located in the hippocampus, was significantly

associated with sight hunting and vermin control ancestry. The hippocampus is part of networks implicated in sight hunting and fear, stress, and anxiety, both significantly linked to sight hunting ancestry in our earlier analysis (Hecht et al. 2019), although the role of vermin control ancestry is more difficult to ascertain at this point. Further research combining structural, functional, and behavioral measures would help elucidate the links between canine brain asymmetries, working functions, age, and sex.

Contrary to our third hypothesis, we did not find support for the proposition that brain asymmetries are a byproduct of brain enlargement. This is notable, given that there was an almost fourfold difference in volume between the smallest and largest brains in our dataset. This contrasts with reports in humans, where brain size does predict the magnitude of asymmetry (Yan et al. 2011; Kong et al. 2018). However, it is important to note that the intense artificial selection which occurred in dog breeds has no correlate in human evolutionary history, and population structure and genetic variation vary markedly between dogs and humans (Norton et al. 2019). Therefore, the present results may suggest that brain asymmetries do not necessarily emerge from increases in brain size in intraspecies contexts where semi-separable lineages have undergone distinct selection pressures on behavior, cognition, and body size. An additional possibility is that positive selection maintains dog brain asymmetries despite variations in brain size.

It is important to acknowledge that the current dataset was opportunistically collected from a veterinary hospital, and while no dogs received a neurological diagnosis and all scans were screened for abnormalities by a veterinary neurologist (M.K.), the sample may not be entirely normative. Additionally, this dataset likely represents companion animals rather than working dogs; it is possible that working training influences dog brain asymmetries. Contrary to our expectations based on human brain asymmetry literature (Kong et al. 2018), we only found evidence for a significant effect of sex on asymmetry in cluster 3, located in the piriform cortex. Since 80.7% of subjects in our sample were spayed or neutered, observable sex effects may have been reduced. We further found no age effects, which contrasts with human reports (Zhou et al. 2013; Kong et al. 2018), and may be related to the fact that only 9 dogs in this dataset were over 10 years of age.

Together, our findings establish dogs as a species for which there are marked structural asymmetries in the gray matter of the brain, much like many primates (Kong et al. 2018; Vickery et al. 2020; Bogart et al. 2012; Marie et al. 2017). This is striking, given that the last common ancestor of carnivorans and primates lived 94 million years ago (Kumar et al. 2017). This either points toward a very deep evolutionary origin for asymmetries in brain organization (Güntürkün et al. 2020) or toward the independent emergence of asymmetries in dogs and primates, paralleling the independent expansion of cortex in these two lineages (Kaas 2011). Either of these possibilities has central relevance for situating the emergence of lateralized functions like language and tool use in our own species within the broader context of the animal kingdom and highlights the utility of dogs for further comparative and evolutionary research on this topic.

3.6 Supplemental Materials

Supplemental materials can be found in the journal *Brain Structure and Function* or in the Appendix.

Chapter 4 Brain-Behavior Differences in Premodern and Modern Lineages of Domestic Dogs

Co-authors: Jeroen B. Smaers, James A. Serpell, and Erin E. Hecht

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4.1 Abstract

Although domestic dogs were the first domesticated species, the nature of dog domestication remains a topic of ongoing debate. In particular, brain and behavior changes associated with different stages of the domestication process have been difficult to disambiguate. Most modern Western breed dogs possess highly derived physical and behavioral traits because of intense artificial selection for appearance and function within the past 200 years. In contrast, premodern dogs, including primitive/ancient breeds, village dogs, and New Guinea Singing Dogs, have undergone less intensive artificial selection and retain more ancestral characteristics. Consequently, comparisons between modern and premodern dogs can shed light on brain and behavior changes that have occurred recently in the domestication process. Here, we addressed this question using a voxel-based morphometry analysis of structural MRI images from 72 modern breed dogs and 13 premodern dogs (32 females). Modern breed dogs show widespread expansions of neocortex and reductions in the amygdala and other subcortical regions. Furthermore, cortical measurements significantly predicted individual variation in trainability, while amygdala measurements significantly predicted fear scores. These results contrast with the long-standing view that domestication consistently involves reduction in brain size and cognitive capacity. Rather, our results suggest that recent artificial selection has targeted higher-order brain regions in modern breed dogs, perhaps to facilitate behavioral flexibility and close interaction and cooperation with humans.

4.2 Significance Statement

This study provides novel insights into the neural changes associated with artificial selection during dog domestication by comparing brain morphology between modern breed dogs and a unique and rare sample of premodern dogs, including ancient breeds, village dogs, and New Guinea singing dogs. Our findings demonstrate that modern breed dogs exhibit significant cortical expansion linked to trainability and premodern dogs show amygdala enlargement associated with heightened fear, suggesting that brain evolution has happened rapidly in a species embedded in the anthropogenic environment.

4.3 Introduction

Dogs were the first species to be domesticated, but the nature of dog domestication remains a topic of intense debate (Thalmann and Perri, 2019). The predominant view is that gray wolves, Canis lupus, initiated their own domestication by scavenging around human settlements (Coppinger and Coppinger, 2001; Larson and Fuller, 2014). However, others argue that hunter-gatherers may have intentionally captured and raised wild wolves to keep as pets, hunting companions, or guards (Germonpré et al., 2021; Serpell, 2021). In either case, behavioral shifts which presumably would have become adaptive during the initial wild-to-domesticate transition include reduced flight-or-fight responses, reduced reactive aggression, and potentially increased behavioral flexibility and learning capacity. These behavioral shifts in early dogs are generally understood to have occurred through natural selection, rather than artificial selection (Scott, 1968; Boyko et al., 2009; Lupo, 2019).

Today, most dogs in the world continue to breed freely (Hughes and Macdonald, 2013; Gompper, 2014). Free-breeding dogs who range freely around human settlements and rely on human waste for survival are termed village dogs (Coppinger and Coppinger, 2001). There are also a few smaller populations of free-breeding dogs, including New Guinea singing dogs (NGSDs), that primarily hunt prey rather than rely on anthropogenic sources of food (Boyko and Boyko, 2014; Surbakti et al., 2020).

However, some dog lineages transitioned from an autonomous lifestyle to one controlled by humans. The oldest dog breeds in existence today are called ancient breeds (Parker et al., 2004; Vonholdt et al., 2010). Unlike modern breeds, ancient breeds were traditionally maintained in open populations without pedigree records and were primarily selected for function, not conformation (Boyko and Boyko, 2014; Worboys et al., 2018).

Modern dog breeding practices began in earnest in the United Kingdom during the Victorian period (Worboys et al., 2018). With the advent of dog clubs, shows, and trials, coupled with scientific advances in animal breeding, people started to systematically breed dogs in closed populations for highly specialized morphologies and behavioral tendencies (Pedersen et al., 2013; Worboys et al., 2018). These modern breeds have been subject to intensive artificial selection (Konno et al., 2016; Hansen Wheat et al., 2019), unlike premodern dogs.

Therefore, premodern dogs, including ancient breeds, village dogs, and NGSDs, offer a window on what early dogs may have been like after the wolf-to-dog transition (Hansen Wheat et al., 2019; Thalmann and Perri, 2019). Comparisons between premodern and modern breed dogs are useful for reconstructing the evolution of traits that are not preserved in skeletal remains, such as the brain and its behavioral output. Behavioral shifts in dog evolution have been a topic of ongoing debate (Marshall-Pescini et al., 2017). On the one hand, domestication is generally presumed to reduce brain size across species (Kruska, 1988; Hecht et al., 2023). Domestication is also generally thought to involve reductions in flight-or-fight responses (Coppinger and Coppinger, 2001; Trut et al., 2009; Zeder, 2012). On the other hand, some argue that modern dogs possess social cognitive capacities which surpass those of extant wolves (Hare et al., 2002; Salomons et al., 2021; but see Range and Marshall-Pescini, 2022), and in at least one population of dogs, intraspecies aggression does not appear to be reduced in dogs relative to wolves (Range et al., 2015). Nearly all behavioral, cognitive, and neuroscience research on dogs to date has focused on modern breeds. Because behavior originates in the brain, comparisons between premodern and modern dogs are necessary to understand selection pressures and behavioral shifts resulting from intensified artificial selection during the late stage of the domestication process.

In this study, we collected T2-weighted MRI scans from 85 dogs of modern and premodern ancestry. Using voxel-based morphometry, we find that modern dog breeds show significant, widespread expansion across cortex, while premodern dogs show significantly larger subcortical structures, particularly the amygdala. Cortical and amygdala expansion are significantly predictive of individual variation in trainability and fear scores, respectively, using the Canine Behavioral Assessment and Research Questionnaire (Hsu and Serpell, 2003).

4.4 Methods

4.4.1 Ethics Statement

All procedures were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) and Internal Review Board (IRB) of Harvard University.

4.4.2 Subjects

Canine subjects were recruited from the Penn Vet Working Dog Center, America's VetDogs, Fidelco Guide Dogs, and private owners. Rather than target-specific breeds, we included all eligible dogs of single breed ancestry and later categorized their modern breed versus premodern status based on available genetic data (Parker et al., 2004) and historical information derived from the “World Atlas of Dog Breeds” (De Vito et al., 2009). Veterinarians screened all candidate subjects prior to inclusion in the study. All subjects were in good health and had no neurological disorders. Dog owners provided informed consent. A total of 85 dogs (32 females) took part in the study, 13 of which were premodern dogs (Supplemental Table 16). All dogs were working and/or companion dogs.

4.4.3 MRI Scan Acquisition

Dogs were anesthetized by a licensed veterinarian during their MRI scans to ensure that they did not experience stress or discomfort from being inside the machine. First, dogs were sedated with butorphanol and dexmedetomidine (0.3 mg/kg +3–5 mcg/kg, i.m.). Next, general anesthesia was induced with propofol (to effect, 2–6 mg/kg, i.v.) and maintained with isoflurane O2. A licensed veterinarian and two veterinary technicians continuously monitored dogs under anesthesia using ECG, SpO2, NIBP (oscillometric), and capnography (InVivo Expression MRI-safe unit). T2-weighted structural images (0.667 mm3, 1 average) were collected. The duration of the scanning was ∼1 h per dog. After the scanning completion, dogs were recovered from anesthesia under the observation of a veterinary technician. Dogs were sent home with a bandana and a framed image of their brain.

4.4.4 Image Processing and Analyses

Data processing was performed with two open-source software packages—FSL (Smith et al., 2004, Jenkinson et al., 2012; https://fsl.fmrib.ox.ac.uk/fsl/fslwiki) and ANTs (Avants et al., 2011; http://picsl.upenn.edu/software/ants/). Brain extraction was accomplished with an in-house pipeline using ANTs (Avants et al., 2011). We generated a study-specific, symmetric template by registering and merging images from 13 premodern dogs with a randomly selected set of 13 modern breed dogs. The images of all subjects were then nonlinearly registered to the template using ANTs (Avants et al., 2011). Bias-field correction and segmentation into gray matter, white matter, and cerebrospinal fluid was accomplished using the FSL FAST tool (Zhang et al., 2001). Total gray matter and white matter volume were added together to determine each subject's total brain volume, which was converted to brain weight in grams.

Each subject's gray matter mask was multiplied by the Jacobian determinant of the ANTS warpfield. This created a Jacobian image containing just gray matter voxels, which is essentially a “heat map” of the spatial transformation that needed to occur to align a subject's brain with the template brain. FSL's randomise tool was then applied to perform Monte Carlo permutation testing of a general linear model comparing whole-brain Jacobian images of modern breed and premodern dogs (Winkler et al., 2014). The threshold used for statistical significance was $p < 0.05$ after threshold-free cluster enhancement (TFCE) for family-wise error correction (Smith and Nichols, 2009).

4.4.5 Brain-Body Allometry Analyses

To determine if premodern and modern breed dogs show different brain–body allometric scaling patterns, a least-squares phylogenetic analysis of covariance (pANCOVA) was performed (Smaers and Rohlf, 2016) using phylogenetic data from Parker et al. (2017). This analysis compared three modern breeds—Labrador retriever, border collie, and German shepherd—with four premodern breeds—saluki, samoyed, Shiba inu, and Siberian husky. Two additional nonphylogenetic versions of this analysis were also performed. The first version consisted of a pANCOVA with a nulled phylogeny, which included all dog types in the dataset. The second version involved two linear regression models—one model with two

intercepts and one slope and another with one intercept. These models were then compared using an ANOVA.

We additionally performed two more voxel-based morphometry analyses to further interpret the findings of our pANCOVA analysis. One voxel-based morphometry analysis investigated the relationship between brain size scaling and regional gray matter expansions and contractions. The other voxel-based morphometry analysis investigated differences in gray matter volume between modern breed and premodern dogs, while controlling for brain size by including it as a covariate.

4.4.6 Canine Behavioral Assessment and Research Questionnaire

The owners of 61 canine subjects (51 modern breed) completed the Canine Behavioral Assessment and Research Questionnaire (C-BARQ; Hsu and Serpell, 2003). Questions 1 through 8 from the trainability subscale were averaged to create a trainability score for each subject (reverse coded items were converted). The same approach was used to generate scores for stranger-directed fear (Questions 36, 37, 39, 40), dog-directed fear (Questions 45, 46, 53, and 54), and nonsocial fear (Questions 38, 41, 42, 44, 47, 48). We also generated an “overall fear” score by averaging questions from all three fear subscales together (Questions 36–54). We generated five separate linear regression models to determine whether each score was significantly predicted by expansions in brain anatomy (Table 6).

4.5 Results

4.5.1 Regional Gray Matter Volume

First, we investigated whether regional gray matter volume across the whole brain varied significantly between 72 modern breed and 13 premodern dogs. Our voxel-based morphometric analysis of T2-weighted images found that modern breed dogs showed expansion throughout the cortex. Specifically, expansions were observed in the frontal gyrus, gyrus rectus, prorean gyrus, composite gyrus, coronal gyrus, precruciate gyrus, postcruciate gyrus, sylvian gyrus, ectosylvian gyrus, suprasylvian gyrus, and marginal gyrus (Figure 11, Supplemental Figure 38, Supplemental Table 17). Additionally, modern breed dogs showed volumetric reductions in subcortical regions, including the amygdala, right nucleus accumbens, hippocampus, and cerebellum (Figure 12, Supplemental Figure 38, Supplemental Table 18).

An additional area of reduction was detected abridging the dorsal aspect of the hypothalamus and ventral aspect of the thalamus surrounding the third ventricle. While the resolution of structural MRI does not allow for precise identification of the borders of hypothalamic and thalamic nuclei, the anatomical location of this cluster is consistent with the nucleus reuniens, paraventricular thalamic nucleus, centromedial thalamic nucleus, posteromedial ventral thalamic nucleus, dorsomedial hypothalamic nucleus, and periventricular hypothalamic nucleus. This cluster extends posteriorly along the gray matter surrounding the third ventricle, consistent with the location of the posterior hypothalamic nucleus and posterior paraventricular hypothalamic nucleus.

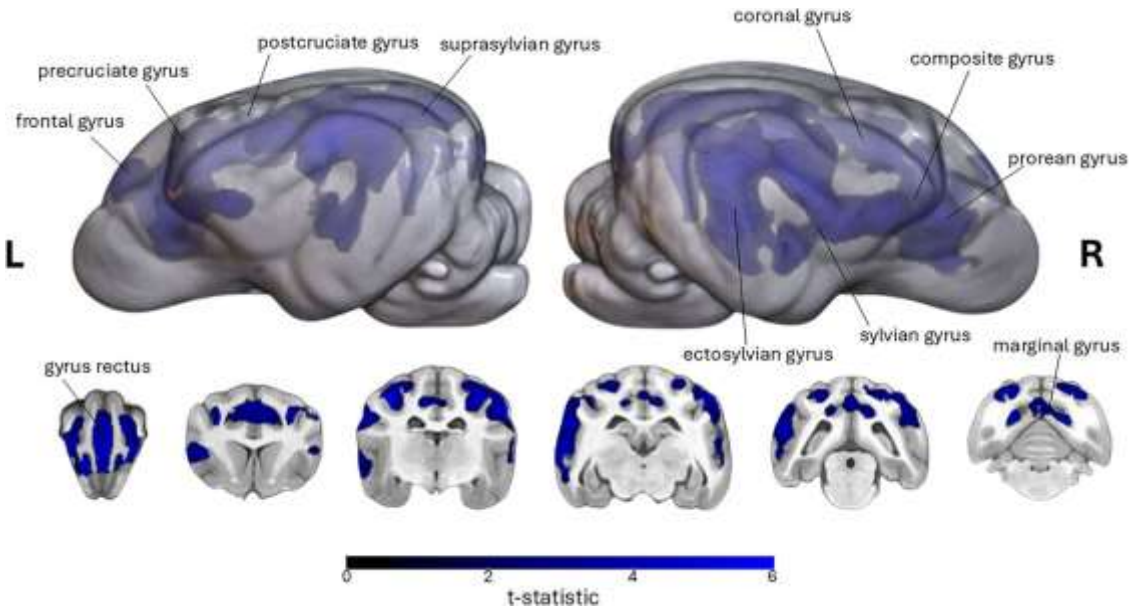


Figure 11. Significantly enlarged regions of gray matter volume in modern breed dogs compared with premodern dogs. Colored regions are all $p < 0.05$ after correction for multiple comparisons; *t* statistic values are illustrated. Visualized on a canine brain atlas created by Johnson et al. (2020).

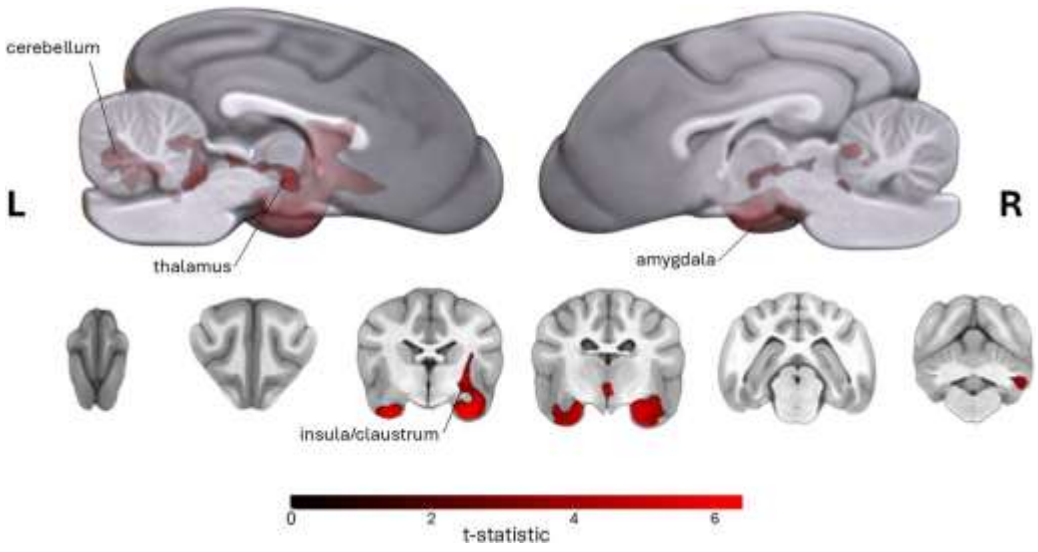


Figure 12. Significantly enlarged regions of gray matter volume in premodern dogs compared with modern breed dogs. Colored regions are all $p < 0.05$ after correction for multiple comparisons; *t* statistic values are illustrated. Visualized on a canine brain atlas created by Johnson et al. (2020).

4.5.2 Brain-Body Allometry

Next, we examined whether premodern and modern breed dogs show different allometric scaling patterns by performing a pANCOVA that incorporated phylogenetic data from Parker et al. (2017). We found no significant difference in the slope or intercept for modern breed versus premodern dogs ($F = 0.49$, $p = 0.65$). Two follow-up analyses using nonphylogenetic approaches found comparable results (both $F = 1.42$, $p = 0.26$).

Although brain volume did not differ significantly between the two groups, we questioned whether variation in brain size might still be significantly associated with variation in regional gray matter morphometry. Previously, we had observed that total brain size largely accounts for variation in cortex volume, which is linked to breed-average trainability (Hecht et al., 2021a). In order to assess the extent to which variation in brain size across modern and premodern dogs accounts for the results observed here, we then performed an additional voxel-based morphometry analysis investigating the relationship between brain size and regional gray matter volume. We found that increased brain size is associated with widespread expansion across the cortex, in regions very similar to those that are expanded in modern breed dogs compared with premodern dogs (Figure 13, Supplemental Figure 39, Supplemental

Table 19). Furthermore, reduced brain size is associated with volumetric reduction in subcortical regions, again very similar to those that are reduced in modern breeds compared with premodern dogs (Figure 13, Supplemental Figure 39, Supplemental Table 20).

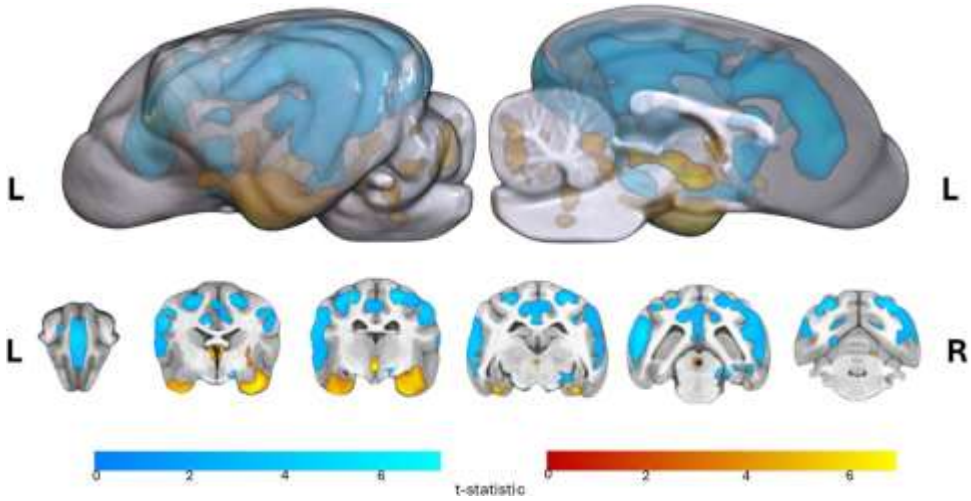


Figure 13. Regions of gray matter volume that are significantly enlarged with increasing brain size (light blue) and decreasing brain size (orange). Colored regions are all $p < 0.05$ after correction for multiple comparisons; *t* statistic values are illustrated. Visualized on a canine brain atlas created by Johnson et al. (2020).

Finally, to assess whether there is any variation in gray matter morphology that is not accounted for by variation in total brain size, we compared regional gray matter differences between premodern and modern breed dogs while controlling for total brain size. We found remaining regions of significant cortical expansion in modern breeds located in parts of the left prorean gyrus, anterior suprasylvian gyrus, and postcruciate gyrus (Figure 14, Supplemental Figure 40, Supplemental Table 22).

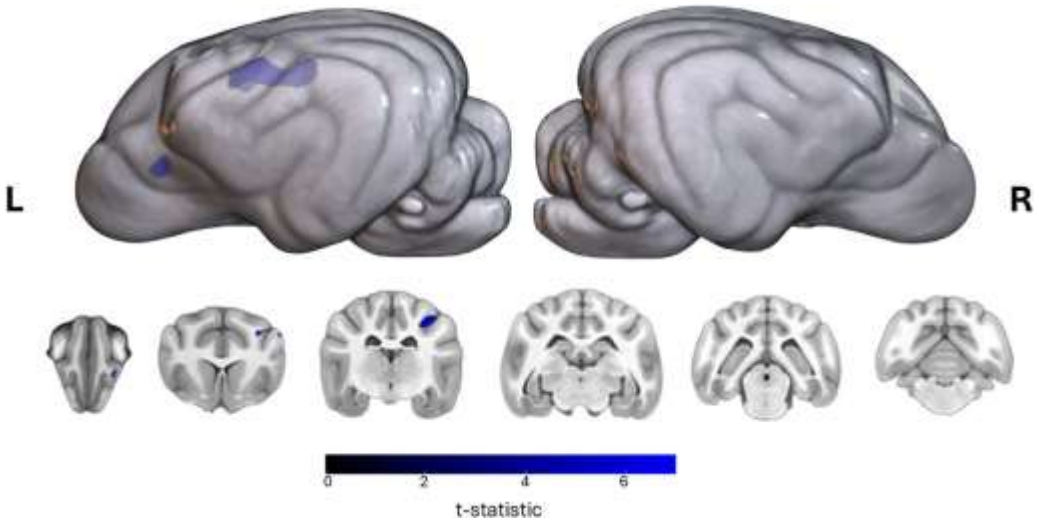


Figure 14. Significantly expanded regions of gray matter volume in modern breed dogs compared with premodern dogs while controlling for brain size. Colored regions are all $p < 0.05$ after correction; *t* statistic values are illustrated. Visualized on canine a canine brain atlas created by Johnson et al. (2020).

4.5.3 C-BARQ Trainability and Fear Scores

Owners of 61 of the dogs in this dataset completed the C-BARQ (Hsu and Serpell, 2003; Duffy and Serpell, 2012). We generated five linear regression models to determine if amygdala/cortical expansion significantly predicts individual C-BARQ trainability, general fear, stranger-directed fear, dog-directed fear, and nonsocial fear scores (Table 6). We found that cortical expansion significantly predicts increased trainability (p = 0.00019, t value = 4.0), while expansion of the amygdala significantly predicts increased overall fear (computed as the average of all C-BARQ fear scales; p = 0.0016, t value = 3.3), stranger-directed fear (p = 1.25 × 10−7, t value = 6.0), dog-directed fear (p = 0.024, t value = 2.3), and nonsocial fear (p = 3.66 × 10−5, t value = 4.5; Figure 15, Table 6). Furthermore, in five additional linear regression models, we found that modern breed versus premodern status significantly predicts individual C-BARQ trainability (p = 3.8 × 10−05, t value = −4.46), overall fear (p = 0.023, t value = 2.34), stranger-directed fear (p = 0.040, t value = 2.11), dog-directed fear (p = 0.041, t value = 2.1), and nonsocial fear scores (p = 0.0166, t value = 2.5; Figure 16, Table 6).

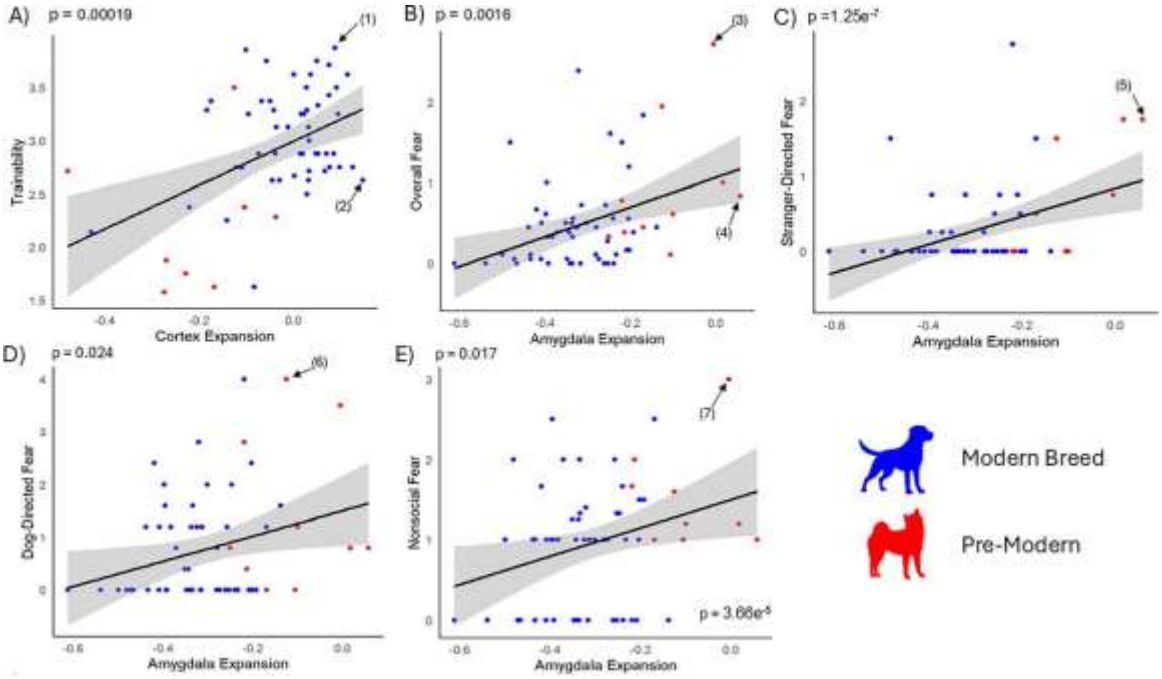


Figure 15. Significantly expanded regions of gray matter volume in modern breed dogs compared with premodern dogs while controlling for brain size. Colored regions are all $p < 0.05$ after correction; *t* statistic values are illustrated. Visualized on canine a canine brain atlas created by Johnson et al. (2020).

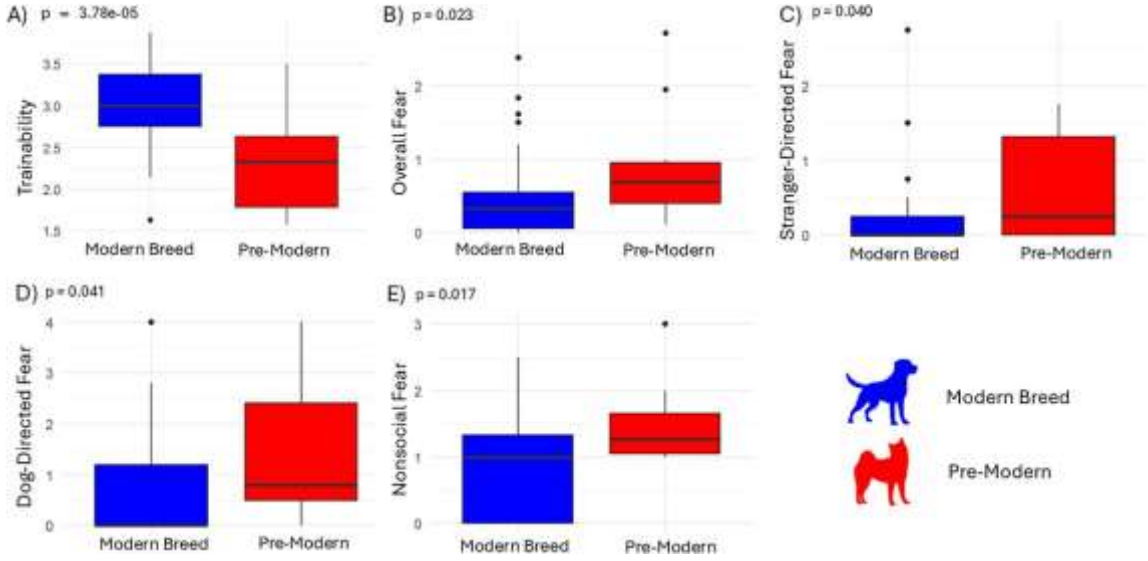


Figure 16. Comparison between modern breed and premodern dogs for C-BARQ scores for trainability (A), overall fear (B), stranger-directed fear (C), dog-directed fear (D), and nonsocial fear (E). p values derived from linear regression models (Table 6).

		Trainability	Overall Fear	Stranger-Directed Fear	Dog-Directed Fear	Nonsocial Fear
Intercept	*p* value	**2×10^{-1}**	**9.98×10^{-07}**	**0.0061**	**2.13×10^{-05}**	**5.87×10^{-12}**
	Estimate	2.04	0.45	0.22	0.67	0.88
	SE	0.070	0.082	0.077	0.15	0.25
	t value	44.03	5.47	2.84	2.1	2.47
Ancestry	*p* value	**3.8×10^{-05}**	**0.023**	**0.040**	0.041	**0.0166**
	Estimate	−0.76	0.47	0.404	0.76	0.63
	SE	0.17	0.20	0.20	0.36	0.25
	t value	−4.46	2.34	2.11	2.1	2.5

Table 6. Summary of linear regression models generated to test the relationship between C-BARQ behaviors and ancestry (modern breed vs premodern status).

4.6 Discussion

The present study investigated differences in relative brain size and regional gray matter volume between modern breed dogs, which have undergone a high degree of artificial selection, and premodern dogs, which have been subject to less intensive artificial selection (Boyko and Boyko, 2014). We performed whole-brain voxel-based morphometry on T2-weighted MRI scans of 85 working and companion dogs. Additionally, owners of 61 of the canine subjects completed the C-BARQ (Hsu and Serpell, 2003), a widely validated assessment of dog behavior. Using these two sources of information, we find evidence that dogs' brains and behaviors have continued to evolve after the initial wolf-to-dog transition.

In our voxel-based morphometry analysis of regional gray matter volume, we found significant and widespread expansion of the cortex in modern breed dogs compared with premodern dogs. This includes large extents of frontal, temporal, parietal, occipital, and cingulate cortex. The cortex is broadly

implicated in higher-order sensory processing, action planning, cognition, and flexible/learned behavior. Given previous findings that modern breed dogs are more trainable than ancient breed dogs (Turcsán et al., 2011 ; Smith et al., 2017), we assessed (1) whether trainability significantly differs between modern breed and premodern dogs and (2) if cortical expansion significantly predicts a dog's trainability score. As expected, modern breed dogs were rated as significantly more trainable than premodern dogs (Figure 13). Furthermore, cortical enlargement positively predicted trainability (Figure 14). These results build upon a previous finding by Hecht and colleagues that there is a significant association between breed-average trainability scores and cortical expansion (2021), although this is the first direct assessment of brain anatomy and trainability ratings within the same individuals. Together, these results suggest that artificial selection in modern breed dogs has acted to increase trainability and cortical volume. Why might this have occurred? In their most common role(s) as household pets and/or working dogs, modern breed dogs interact closely with humans. This niche may have favored dogs with larger, more plastic cortices that were better able to learn novel behaviors and skills from humans. Consistent with this interpretation, the dogs with the highest trainability scores and greatest cortical expansion were purpose-bred working dogs (Figure 14). Brain tissue is metabolically expensive (Aiello and Wheeler, 1995), which generally limits brain enlargement across species (Isler and van Schaik, 2014), but since household pets and working dogs are well provisioned and have a stable diet, their brains may have been released from this constraint (Hecht et al., 2023).

Compared with premodern dogs, modern breeds also show gray matter reduction in several subcortical structures, most markedly including the amygdala (Figure 12). The amygdala processes both positive and negative environmental stimuli but is especially well-known for its role in fear learning (Janak and Tye, 2015). In a post hoc analysis, we further discovered that expansion of the amygdala significantly predicts owner-reported overall fear (computed as an average of all C-BARQ fear scores), stranger-directed fear, dog-directed fear, and nonsocial fear (Figure 15, Table 6). Our findings are therefore consistent with the idea that the flight-or-fight response may have been targeted by selection over the course of dog domestication (Price, 1984), not just in the initial transition of early modern dogs from a now-extinct wolf ancestor, but also in more recent, ongoing selection after domestication had occurred. Premodern dogs may have historically benefited from having elevated fear levels as they lived more

independently from humans and may have needed to evaluate and avoid threats in the environment by themselves. On the other hand, modern breed dogs have evolved to be highly integrated into human society, and survival in this environment might require reduced fearfulness. Humans may also directly select against behaviors resulting from flight-or-fight processing, particularly in the case of working dogs, where these behaviors can conflict with work goals. Notably, portions of the hypothalamus, which is also centrally involved in flight-or-fight processing, were also reduced in modern breed dogs (Figure 12).

To evaluate whether relative brain size is different between modern breed and premodern breed dogs, we conducted a pANCOVA (Smaers and Rohlf, 2016). This analysis did not show a significant difference in relative brain size between modern breeds and premodern dogs. Additional nonphylogenetic analyses produced the same result. However, when we subsequently performed a whole-brain voxel-based morphometry analysis investigating the relationship between total brain size and regional gray matter volume, we found widespread cortical expansion and contraction of the amygdala with increasing brain size, closely mirroring modern/premodern differences (Supplemental Figure 40). Therefore, while relative brain size differences between premodern and modern dogs did not reach significance in this sample, variation in absolute brain size between these two groups accounts for nearly all of the variation in regional brain anatomy. This is consistent with the “late equals large” hypothesis by Finlay and colleagues, which proposes that as brains scale larger, late-developing cortex disproportionately expands, while earlier developing regions, including the amygdala, disproportionately shrink (Finlay et al., 2001).

Interestingly, though, even after controlling for total brain size, some regions of cortex are still significantly larger in modern breed dogs. This is suggestive of focal, mosaic adaptation which occurs on top of the backdrop of global, concerted, allometric change (Striedter and Northcutt, 2019). These regions include portions of the postcruciate gyrus (motor cortex), anterior suprasylvian gyrus (temporal cortex), and prorean gyrus (prefrontal cortex). Notably, the prorean gyrus is implicated in the emergence of cooperative pack hunting in the carnivore lineage (Radinsky, 1969) and has been affected by selection on social behavior in the Russian farm-fox model (Hecht et al., 2021b). The anterior suprasylvian gyrus activates in response to spoken human language in awake dog fMRI studies (Andics et al., 2016; Cuaya

et al., 2022; Bálint et al., 2023). Together, this suggests that cortical areas supporting social cognition and social communication have been under specific positive selection in modern breeds.

An additional possibility is that experiential differences between modern and premodern dogs in this dataset may account for a portion of the observed neuroanatomical variation, as some of the modern breed dogs were enrolled in working dog training programs. However, our results cannot be attributed entirely to plasticity effects for several reasons. First, we previously observed a link between cortical expansion and trainability scores in a study that assessed neural correlates of breed-average C-BARQ scores (Hecht et al., 2021a); this prior analysis was blind to individual variation in experience and driven entirely by heritable, breed-level traits. Second, the brain–behavior associations we report here occurred in both working and nonworking individuals. And third, the anatomical extent and magnitude of the current results far exceed any prior report of experience-dependent plasticity and are more in line with innate, heritable traits. The effect of specific training experiences on brain organization is an important question for future research.

There are several limitations of our study that should be noted. First, the ancestral population of early domestic dogs is extinct and their brains and behavior are not available for study. Today's premodern dogs are not “living fossils,” although they presumably possess more ancestral traits than highly derived, artificially selected modern breeds. Second, there are additional lineages of premodern and modern dogs which are not represented in this sample and should be examined in future research, along with variation among breeds/types within each group. Additional important topics for future research include examining other aspects of brain organization, such as connectivity patterns and cell type distributions, as well as underlying genetic architecture.

Together, our findings suggest that the brain–behavior phenotype of recent dog domestication involves reduction in flight-or-fight processing, as mediated by the amygdala, as well as increases in learning and behavioral flexibility, as mediated by distributed cortical regions. Interestingly, these neural changes are paralleled in rabbit domestication (Brusini et al., 2018). Our results are consistent with a dual-phase model of dog domestication which posits early attenuation to the human socio-ecological niche followed by additional adaptative changes supporting behavioral specialization for particular

contexts within that niche (Tancredi and Cardinali, 2023). Our findings challenge the long-standing idea that domestication consistently involves reductions in brain size (Kruska, 1988). Furthermore, our results are consistent with the emerging pattern that brain evolution in domestic dogs has been shaped by both concerted developmental patterning in brain scaling (Finlay et al., 2001; Hecht et al., 2021a) and by focal, mosaic change (Hecht et al., 2019). While dogs were the first species domesticated by humans, they are far from the only ones. Among mammals, the biomass of domesticates now far outweighs that of wild species by 2 orders of magnitude (Bar-On et al., 2018), and increasing anthropogenic influence is arguably now a significant selective force for all animals on the planet. Thus, our results raise the possibility that comparable neuro-evolutionary changes may also be occurring in other animals and further research is warranted in additional species.

4.7 Supplemental Materials

Supplemental materials can be found online in the Journal of Neuroscience or in the Appendix.

Chapter 5 White matter differences in the brains of modern and premodern dogs

Co-Authors: Isabel Levin, Jayvier Plaza Hernández, Katie Dabney, and Erin Hecht

5.1 Abstract

Linking variation in brain structure to variation in behavior remains a central challenge in neuroscience. Domestic dogs provide a powerful within-species model because modern breeds and premodern dogs have experienced markedly different selective pressures on social cognition and learning. Here, we tested whether recent, behavior-focused artificial selection in modern breed dogs is associated with systematic divergence in white matter organization relative to premodern dogs. We acquired T1-weighted, T2-weighted, and diffusion-weighted MRI from 52 dogs (29 modern breed, 23 premodern) and applied tract-based spatial statistics (TBSS), and whole-brain probabilistic tractography with graph-theoretical analyses. Modern breed dogs exhibited significantly greater fractional anisotropy (FA) across large, distributed clusters spanning cerebral white matter as well as thalamic and midbrain regions, whereas no regions showed greater FA in premodern dogs. FA within modern-enriched clusters

positively predicted C-BARQ trainability scores across individuals. Network analyses demonstrated altered global topology in modern dogs, including reduced weighted clustering coefficients, distinct community organization, and increased cortical hub prominence, whereas premodern dogs showed greater relative subcortical connectivity. Together, these findings indicate that recent artificial selection for cooperative learning and trainability is associated with large-scale reorganization of the canine connectome. Even over short evolutionary timescales within a single species, selection on behavior can substantially reshape structural brain connectivity.

5.2 Introduction

A central challenge in neuroscience is linking variation in brain structure to variation in behavior (Genon et al., 2022). Domestic dogs offer a rare opportunity to investigate this question, as they exhibit extraordinary behavioral diversity within a single species. Following the initial wolf-to-dog transition, some dog populations experienced relatively weak or indirect artificial selection, while others underwent intense, intentional selection for specialized behavioral roles (Boyko & Boyko, 2014; Pongrácz & Dobos, 2025). This provides a powerful natural experiment for addressing how selection for behavior, particularly traits central to life in the human social niche such as cooperation, learning, and reduced reactivity, can drive systematic divergence in brain organization over short evolutionary timescales.

Modern breed dogs were developed in Western societies over the past two centuries through directional selection for appearance and/or behavior (Parker et al., 2017). During this period, formalized kennel clubs, breed registries, and working dog organizations emerged, which standardized breed definitions and codified selective breeding practices (Coutts & Harley, 2010; Larson et al., 2012; Worboys et al., 2018). As a result, modern dogs diversified into specialized breeds optimized for specialized roles within human societies (Dutrow et al., 2022). Importantly, many of these roles require close affiliation and cooperation with humans, as is the case for herding, retrieving, and companionship (Bognár et al., 2021; Höglin et al., 2021; Miklósi et al., 2021).

In contrast to modern breed dogs, older lineages of dogs from outside the West have experienced less intensive artificial selection (Boyko & Boyko, 2014; Trut et al., 2021). These premodern dogs include ancient breed dogs, such as Siberian huskies and salukis, as well as village dogs (also

known as free-ranging dogs or FRDs) (Barton et al., 2025; Geiger et al., 2017). Ancient breeds descend from landraces that predate Victorian breed formation and were shaped by a mixture of natural and artificial selection (Boyko & Boyko, 2014; Skabelund, 2011; Smith et al., 2017). Village dogs inhabit human settlements but roam and breed freely, thereby experiencing natural and sexual selection (Car et al., 2025; Pilot et al., 2016). Notably, neither ancient breed nor village dogs underwent strong selection for close coordination with humans as modern breed dogs have (Höglin et al., 2021). It has therefore been argued that ancient breed (Hansen Wheat et al., 2019) and village dogs (Car et al., 2025) are good approximate models of what early domestic dogs may have been like, although it is important to remember that they are not “living fossils” and may still have derived phenotypes (Barton et al., 2025).

While premodern dogs are known for their closer genetic affinity to gray wolves (Lin et al., 2025), seasonal breeding (Fielding et al., 2021; Gardner et al., 2025; Kolkmeyer et al., 2024; Tedor & Reif, 1978), and howling (Lehoczki et al., 2023), modern breed dogs have been found to be more trainable (Smith et al., 2017; Turcsán et al., 2011), have stronger social learning abilities (Pongrácz & Dobos, 2025), and more synchronized with their owner (Höglin et al., 2021; Kujala et al., 2023). Some of these traits, such as trainability, might be rooted in neural divergence between modern breed and premodern dogs.

Indeed, dogs with greater genetic distance to wolves have relatively larger brains, as measured via endocasts (Garamszegi et al., 2023). Our group has published complementary work that has shown that modern breed dogs have expanded cerebral cortex relative to premodern breed dogs, who in turn have expanded subcortical regions (Barton et al., 2025). Importantly, cortical expansion was significantly associated with increased trainability, whereas amygdala expansion was significantly correlated with increased fear (Barton et al., 2025)

Because gray and white matter co-develop and co-evolve (Zhang & Sejnowski, 2000), differences in overall brain size are expected to be accompanied by corresponding differences in white matter organization. As brains increase in size, total white matter volume also increases, but it scales sublinearly relative to the expansion of the cerebral cortex (Ardesch et al., 2022). This disproportionate scaling imposes constraints on long-range connectivity, such that larger brains contain a lower proportion of long-

distance connections relative to shorter, more local ones (Ardesch et al., 2022). To preserve efficient information processing under these wiring constraints, larger brains tend to adopt more modular and segregated network architectures (Puxeddu et al., 2024). They also tend to invest more in myelination as an energy-saving adaptation (Wang et al., 2008). Given that modern breed dogs have relatively larger brains than premodern dogs (Garamszegi et al., 2023), they may be expected to exhibit corresponding shifts in white matter organization consistent with these general scaling principles.

The present study tests this prediction by directly comparing white matter organization between two major dog lineages—modern breed dogs and premodern dogs. Using T1-weighted, T2-weighted, and diffusion-weighted MRI from 52 dogs, we quantified white matter differences using complementary approaches, including whole-brain probabilistic tractography, tract-based spatial statistics, and T1w/T2w ratio mapping. Together, these analyses allow us to assess whether recent, behavior-focused artificial selection in modern breed dogs is associated with systematic divergence in white matter organization relative to premodern dogs, providing insight into how selection on behavior can shape brain connectivity over short evolutionary timescales.

5.3 Methods

5.3.1 Ethics Statement

All procedures were reviewed and approved by the IRB and IACUC of Harvard University.

5.3.2 Subjects

Dogs were recruited from the United States using social media and local advertising around the Harvard area. All dogs were privately owned companion, working, or service animals. Village dogs from Africa and Eurasia were brought into the United States by nonprofit organizations or American citizens for them to be adopted as pets. The sample included 23 premodern dogs (5 village dogs and 18 ancient breed dogs) and 29 modern breed dogs. For the purpose of this study, the New Guinea Singing Dog is considered an ancient breed dog, as New Guinea Singing Dogs were brought to the US in the 1950s and have been kept in captivity and bred within a closed pool here since that time (ref), although this is somewhat of a liminal case. **Table 7** provides subject details. Importantly, dogs from both the premodern

and modern group were involved in dog sports and specialized working behaviors. **Figure 17** shows photographs of some of the subjects.

Figure 17. Subjects: (A) Premodern dogs. First row, left to right: Fattoush, Lebanese village dog; Kismet, Seppala Siberian Sled Dog and Apollo, Siberian Husky; Charlie, Chinese village dog; Kopi, New Guinea singing dog; Mochi, Shiba Inu. Second row, left to right: Yelena, Samoyed; Sugar, Indian village dog; Kaede, Kishu Ken; Kirby, Korean Village Dog; Sakura, Kishu Ken. (B) Modern breed dogs. First row, left to right: Nero, German Shepherd; Nikko, Border Collie; Westley, Labrador Retriever; Pasta, Border Collie; Caroline, Labrador Retriever. Second row, left to right: Billy, Labrador Retriever; Tamsin, American Pit Bull Terrier x Australian Shepherd x American Staffordshire Terrier x Labrador Retriever x Boxer x Rottweiler x American Bulldog x Bullmastiff x Boston Terrier; Buck, German Shepherd; Maxine, Labrador Retriever; Lenna, Border Collie.

Name	Group	Breed/type	Age	Sex	Neuter status	Working/sporting activities
Dima	Modern breed	Border collie	2.3	Female	Desexed	None
Harley	Modern breed	Labrador retriever	1.3	Male	Desexed	Service work
Westley	Modern breed	Labrador retriever	1.3	Male	Desexed	Service work
Lenna	Modern breed	Border collie	7	Female	Desexed	Herding livestock
Raven	Premodern	West Siberian laika	2	Female	Intact	Barn hunt
Pochacco	Premodern	Samoyed	3.6	Male	Inact	Rally, barn hunt
Chichy	Modern breed	Labrador retriever	3	Female	Desexed	Service work
Pasta	Modern breed	Border collie	2.08	Male	Desexed	Herding livestock
Cue	Modern breed	Labrador retriever	2.5	Female	Desexed	Service work
Kopi	Premodern	New Guinea singing dog	1.5	Female	Intact	Barn hunt
Oona	Premodern	Siberian husky	8	Female	Desexed	None
Vanda	Modern breed	Border collie	8.4	Female	Desexed	None
Cap	Modern breed	Border collie	11	Male	Intact	Herding livestock
Kaede	Premodern	Kishu ken	2.8	Male	Intact	Barn hunt, weight pull
Yelena	Premodern	Samoyed	1.4	Female	Intact	None
Sakura	Premodern	Kishu ken	1.8	Female	Intact	Barn hunt, weight pull
Sugar	Premodern	Indian village dog	3.5	Female	Desexed	None
Milktea	Premodern	Shiba inu	3.3	Female	Desexed	None
Levi	Modern breed	German shepherd	2.4	Male	Desexed	Guide work
Raella	Modern breed	German shepherd	1.9	Female	Desexed	Guide work
Buck	Modern breed	German shepherd	1.8	Male	Intact	Protection work, service work
Dak	Modern breed	German shepherd	3.8	Male	Intact	Protection work
Billy	Modern breed	Labrador retriever	8.8	Male	Intact	Hunting fowl
Tamsin	Modern breed	American Pit Bull Terrier x Australian	7.3	Female	Desexed	None

		Shepherd x American Staffordshire Terrier x Labrador Retriever x Boxer x Rottweiler x American Bulldog x Bullmastiff x Boston Terrier				
Tatanka	Premodern	Siberian husky	2.9	Male	Desexed	None
Tuktuk	Premodern	Siberian husky	5.8	Male	Desexed	None
Zeeba	Premodern	Saluki	8.6	Male	Desexed	None
Argus	Modern breed	Labrador retriever	0.8	Male	Intact	Scent detection
Polka	Modern breed	Labrador retriever	4.4	Female	Desexed	None
Ryan	Modern breed	Labrador retriever	5.2	Male	Desexed	None
Caroline	Modern breed	Labrador retriever	5.7	Female	Desexed	None
Daisy	Modern breed	Labrador retriever	4.7	Female	Desexed	None
Coco	Modern breed	Labrador retriever	4	Female	Desexed	None
Tartan	Modern breed	Labrador retriever	3.8	Male	Desexed	None
Maxine	Modern breed	Labrador retriever	1.1	Female	Intact	Hunting fowl
Angel	Modern breed	Labrador retriever	4.3	Female	Desexed	None
Spud	Modern breed	Labrador retriever	1.7	Female	Intact	Hunting fowl
Grey	Modern breed	Labrador retriever	6.2	Male	Desexed	None
Remy	Modern breed	German shepherd	2.9	Male	Desexed	None
Dami	Premodern	Samoyed	2.08	Female	Intact	Barn hunt, herding livestock
Rexxar	Modern breed	Border collie	0.92	Male	Intact	None
Charlie	Premodern	Chinese village dog	3	Male	Desexed	None
Mochi	Premodern	Shiba inu	5.58	Female	Desexed	None
Chalupa	Premodern	Samoyed	1.42	Male	Desexed	None
Fattoush	Premodern	Lebanese village dog	8	Male	Desexed	None

Apollo	Premodern	Siberian husky	6.17	Male	Desexed	Sprint sled dog racing
Kismet	Premodern	Seppala Siberian sled dog	1.75	Female	Intact	Sprint sled dog racing
Nikko	Modern breed	Border collie	1.08	Male	Intact	None
Kirby	Premodern	Korean village dog	5.5	Male	Desexed	Agility, scent detection
Vanilla	Premodern	Malawian village dog	6.42	Male	Desexed	None
Julian	Premodern	New Guinea singing dog	4	Male	Desexed	None
Rymoka	Premodern	New Guinea singing dog	10	Female	Desexed	None

Table 7. Subject details. Age is given in years.

5.3.3 MRI Scan Acquisition

To alleviate stress associated with the scanner environment, dogs were anesthetized during data collection. Scans were supervised by licensed veterinarians. The anesthesia protocol was as follows: sedation with butorphanol and dexmedetomidine (0.3 mg/kg + 3-5 mcg/kg IM); anesthesia induction with propofol (to effect, 2-6 mg/kg IV) and maintenance with isoflurane (100% O¬2). An InVivo Expression MRI-safe unit was used to continuously monitor dogs throughout anesthesia, including ECG, SpO2, NIBP (oscillometric), and capnography. A Siemens 3.0 Tesla MAGNETOM Prisma MRI unit and a Siemens 15-channel TX/RX knee coil were used to acquire images. Sequences acquired for this study included T1-weighted images (0.67 mm3, 2 averages); T2-weighted structural images (0.67 mm3, 1 average); and diffusion-weighted images (1.30 mm3, 60 diffusion directions, 2 averages acquired with reversed phase encoding, 12 B0s), lasting approximately 1 hour per dog. After data acquisition was complete, dogs were recovered from anesthesia under veterinary supervision, reunited with their owners, and were given a framed image of their brain and a bandana.

5.3.4 Image Processing

Image preprocessing and analysis used the FSL software package (Smith et al., 2004; Woolrich et al., 2009; Jenkinson et al., 2012). Brains were isolated from raw images, and structural images were segmented and bias-corrected using the FSL FAST tool (Zhang et al., 2001). Diffusion images were processed using TOPUP for EPI distortion correction, EDDY for eddy current correction, DTI fit for tensor

fitting, BEDPOSTX to generate a probabilistic distribution of fiber population orientations, and probtrackx2 for tractography (Andersson et al., 2003; Behrens et al., 2003; Behrens et al., 2007). We used the ANTS software package for registration (Avants et al., 2009a; Avants et al., 2009b). Rigid body alignments were computed between subjects' diffusion data and their structural images. Nonlinear transformations were computed between subjects' structural images and the template.

5.3.5 Tract-Based Spatial Statistics

We applied a modified version of FSL's TBSS pipeline (Smith et al., 2006) in order to use ANTS nonlinear transforms rather than FSL's *fnirt* transforms, which are less precise. Subjects' native-space FA images eroded to remove edge voxels, brought into the study-specific standard space using ANTS, and skeletonized (which projects FA values into a common skeletal frame across all subjects), and thresholded at FA > 0.2. FSL's randomise tool was then used to apply a general linear model with Monte Carlo permutation testing; multiple comparisons correction was accomplished via threshold-free cluster enhancement (TFCE) at $p < .05$ (Winkler et al., 2014). This shuffles the group assignments across subjects (modern breed or premodern) for 5,000 permutations to build up a null distribution of expected t statistics when there is no true association between FA and group. The t statistic values for the true group assignments are then compared across the brain to this null distribution in order to identify voxels where FA differed significantly between modern breed and premodern dogs. We applied threshold-free cluster enhancement for family-wise error correction.

In one generalized linear model (GLM) we analyzed the relationship between C-BARQ trainability and average FA of the significant TBSS cluster. In another GLM we examined the relationship between trainability and modern breed versus premodern dog group status.

The Cornell Canine Brain Atlas (Johnson et al., 2020) was used to create 234 binarized ROI masks which are based on myleoarchitectonic segmentations (Kreiner, 1962, 1964a, b, c, 1966). Tractography was run between all pairwise combinations of ROIs for each subject using FSL's BEDPOSTX and probtrackx functions with a white matter waypoint mask. Waytotals were divided by the volumes of the seed ROIs to correct for ROI size and symmetric individual connectivity matrices were created. These matrices were turned into undirected graph networks with nodes representing gray matter

ROIs and edges representing volume-corrected waytotals. These networks were analyzed in Python using the NetworkX package (Aric et al., 2008) and visualized in Gephi (Bastian et al., 2009). Global statistics were calculated for each individual and pairwise t-tests were performed to assess differences between premodern and modern groups.

Group average matrices were created for premodern dogs and modern dogs. Global statistics and community detection were run. Communities were created using NetworkX's Louvain Community Detection Algorithm, a heuristic method using modularity optimization (Blondel et al., 2008). A Jaccard Similarity Index was calculated for premodern versus modern dogs. For both modern and premodern groups, networks were visualized in Gephi and community masks were created in FSL and visualized in MRIcroGL.

Hubs were defined as ROIs in the top 20% in both betweenness centrality and weighted degree (Sporns et al., 2007; Buckner et al., 2009; Bullmore and Sporns, 2009; van den Heuvel and Sporns, 2013) using Gephi. Hubs were visualized in MRIcroGL. ROIs showing the greatest percentage difference in weighted degree between groups were also calculated to find the top 5 ROIs showing increased connectivity in premodern dogs and the top 5 ROIs showing increased connectivity in modern dogs.

5.4 Results

5.4.1 TBSS Analysis

No voxels showed significantly greater fractional anisotropy (FA) in premodern dogs than in modern dogs.

Modern breed dogs showed significantly greater FA in two large, distributed clusters. These spanned large extents of the cerebral white matter, along with white matter in the thalamus, ventral forebrain, and midbrain (**Figure 18**; **Table 8**). Fractional anisotropy (FA) within these clusters significantly correlated with C-BARQ trainability scores across individual dogs ($\beta = 8.505$, SE = 2.418, $t = 3.517$, $p = 0.00104$; **Figure 18B**). Premodern dogs were significantly less trainable than modern breed dogs ($\beta = -0.729$, SE = 0.159, $t = -4.59$, $p = 3.89e\text{-}5$; **Figure 18B**).

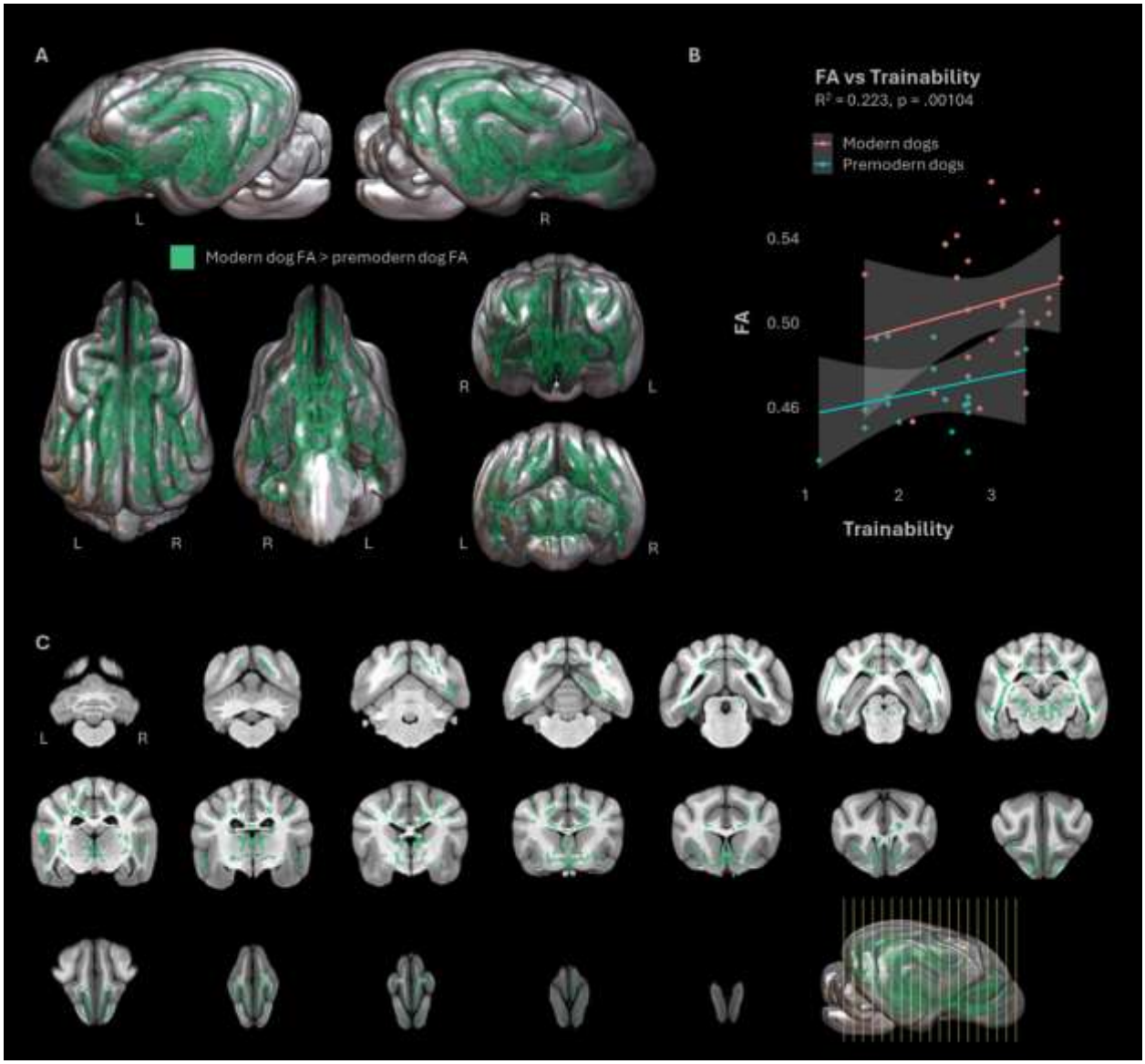


Figure 18. Fractional anisotropy (FA) is significantly increased in widely distributed portions of cerebral white matter in modern dogs compared to premodern dogs. (A) 3D rendered views of TBSS result showing voxels where FA is significantly increased in modern dogs. (B) FA within these voxels is significantly correlated with C-BARQ trainability scores in both modern and premodern dogs. (C) 2D coronal planar views of result in (A).

Cluster Index	Volume	Max T-stat	Max X	Max Y	Max Z	COG X	COG Y	COG Z
2	19021	6.71	65	112	32	60.4	98.1	45.6
		6.71	65	112	32			
		5.96	59	119	40			
		5.77	56	131	31			

		5.65	53	49	69			
		5.6	61	112	33			
		5.58	57	127	34			
1	4692	5.85	39	111	72	63.6	93.2	72.3
		5.85	39	111	72			
		5.62	77	88	73			
		5.16	37	113	73			
		5.01	37	116	71			
		4.69	35	122	69			
		4.68	75	85	72			

Table 8. Volume, maximum t-statistic values and coordinates, and center of gravity (COG) coordinates for TBSS results shown in Figure 18. Coordinates and volumes are given in voxels in the Johnson canine template space.

5.4.2 Connectivity Network Analyses

There was a statistically significant difference in weighted clustering coefficient between modern dogs and premodern dogs ($t(22) = -2.90$, $p = 0.006$). Community organization was noticeably different between modern and premodern groups. Eight communities were found in modern breeds, while only seven were found in premodern dogs (**Figure 19)**. In modern dogs, unlike premodern dogs, the cerebellum, superior colliculus, and inferior colliculus form their own distinct community (**Figure 19b**).

The other distinct shift in community structure involves the composition of frontal, sensory-motor, and olfactory bulb clustering. In premodern dogs, these regions form one large community in the right hemisphere and two distinct communities in the left. In modern dogs, this pattern is reversed: one large community is formed in the left hemisphere and two distinct ones form in the right.

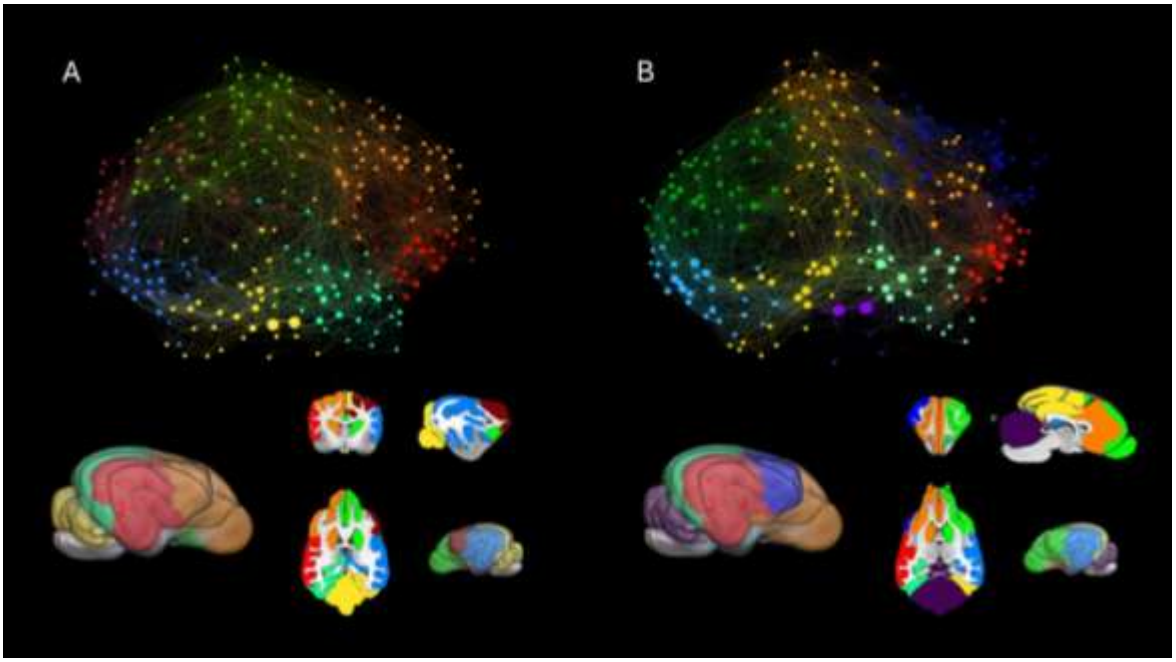


Figure 19. Networks and communities. (A) Premodern dogs. (B) Modern breed dogs.

Hub structure is mostly consistent between premodern and modern breeds, with some unique hubs apparent for each group (**Figure 21**). Distinct differences can be seen in frontal regions which are hubs in modern dogs only and in certain subcortical regions which are hubs in premodern dogs only. Hubs which were present in both lineages include the caudate nucleus, the right hippocampus, olfactory bulb, marginal gyrus, medial occipital gyrus, the posterior entolateral gyrus, the posterior ectolateral gyrus, the medial suprasylvian gyrus, and the dorsal ectosylvian gyrus. Hubs which were unique to premodern dogs were the left hippocampus (subcortical), the right dorsal presplenial gyrus (parietal), the right splenial fissure (occipital), and the right medial posterior composite gyrus (temporal). Hubs which were unique to modern dogs were all sensorimotor regions: the left anterior coronal gyrus and the coronal fissure in both hemispheres.

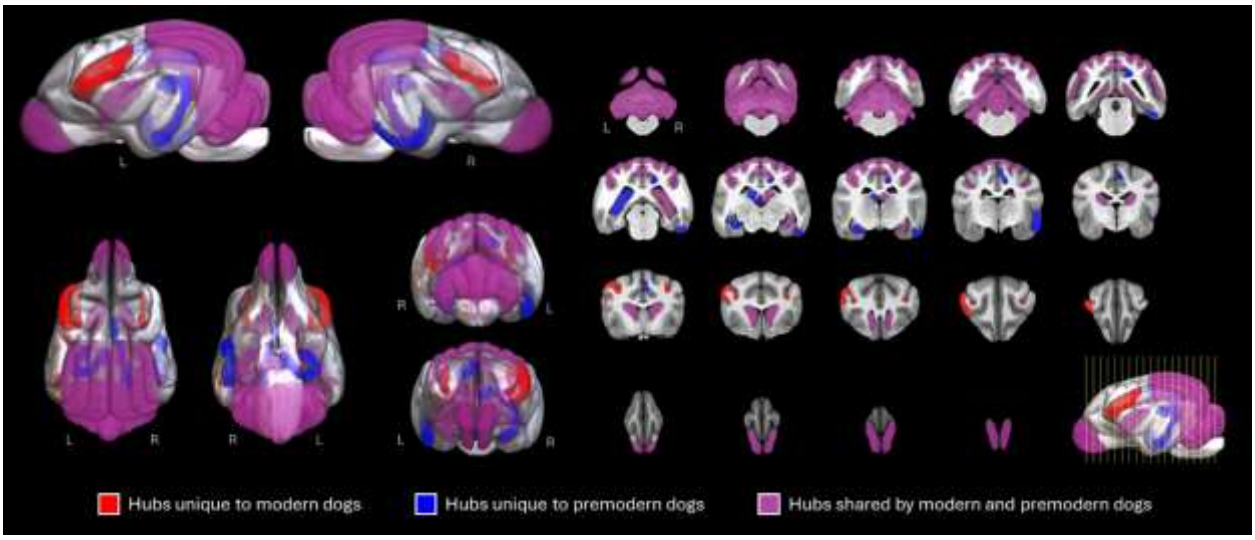


Figure 20. Network hubs in modern breed and premodern dogs.

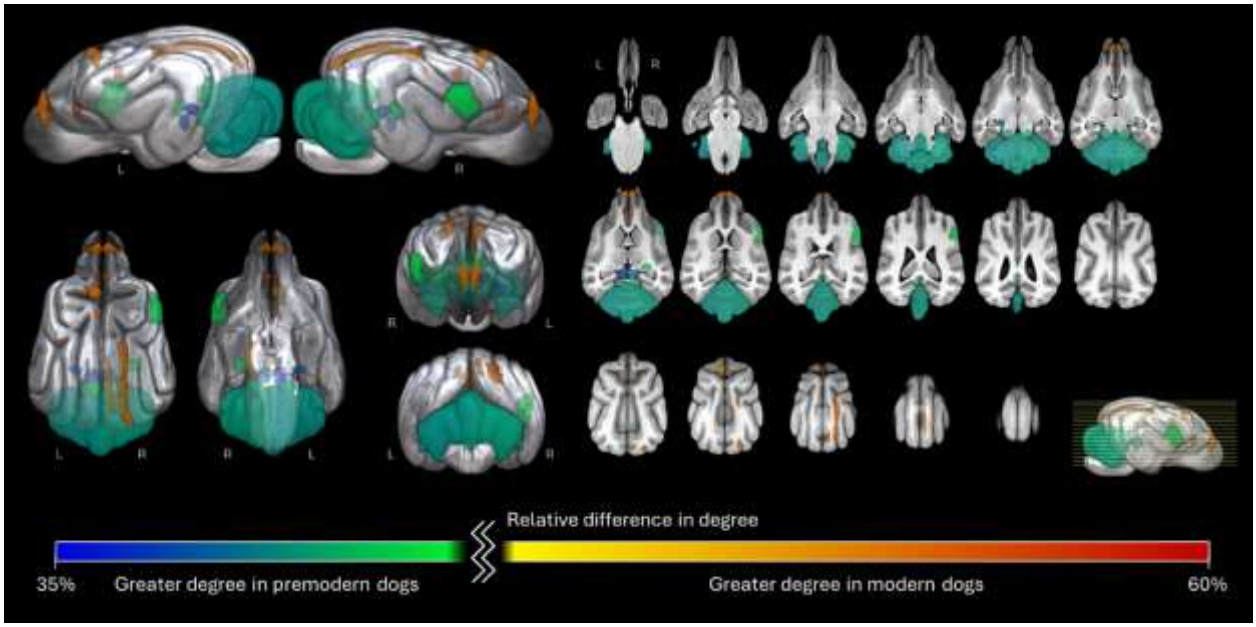


Figure 21. Regions with the greatest difference in degree between premodern and modern dogs.

5.5 Discussion

Modern breeds of dogs created in the past 200 years have evolved derived traits in response to artificial selection (Akey et al., 2010; Parker et al., 2017). In contrast, premodern dogs, including free-ranging village dogs and ancient breed dogs, have experienced less artificial selection (Pilot et al., 2016; Smith et al., 2017). This presents a rare opportunity to investigate brain-behavior evolution within a single species. Previously we found that cerebral gray matter volume is expanded in modern breed dogs relative

to premodern dogs, while subcortical structures including the amygdala are larger in premodern dogs relative to modern breed dogs (Barton et al., 2025). To examine whether white matter organization also differs between the two lineages, we collected T1, T2, and diffusion weighted brain scans from 29 modern breed and 23 premodern dogs. We used tract-based spatial statistics to assess FA and connectivity network analysis to assess global connectivity patterns. We find that white matter organization differs systematically between modern breed and premodern dogs.

Modern breed dogs showed significantly greater FA across large, distributed white matter clusters, with no regions showing greater FA in premodern dogs. These clusters spanned extensive portions of cerebral white matter as well as thalamic and midbrain regions, indicating broad microstructural divergence between the two groups. Critically, FA within these clusters was significantly and positively correlated with C-BARQ trainability scores across individual dogs. This association suggests that increased white matter integrity, often interpreted as reflecting greater axonal coherence, packing density, and/or myelination (Beaulieu, 2002), may support enhanced efficiency of long-range communication among cortical regions involved in learning and social responsiveness (Hecht et al., 2015, 2023)

At the level of large-scale network organization, connectivity analyses revealed that these microstructural shifts are accompanied by altered global topology and nodal organization. Modern breed dogs exhibited significantly lower weighted clustering coefficients than premodern dogs, indicating a shift in the balance between local segregation and distributed integration. Community detection further revealed divergent global architecture: modern breed dogs had eight communities, including a distinct cerebellar-collicular module not segregated in premodern dogs, which instead formed seven communities overall. This shift in network topology is consistent with known scaling principles – the connectome becomes progressively more modular as brain volume increases (Puxeddu et al., 2024). Nodal analyses showed that regions exhibiting the largest increases in weighted degree in premodern dogs were predominantly subcortical, whereas modern breed dogs showed the largest increases in cortical regions, particularly frontal and parietal areas. Unique frontal and sensorimotor hubs in modern breed dogs contrasted with unique subcortical hubs in premodern dogs.

From a broad perspective, our findings indicate that relatively smaller premodern dog brains allocate proportionally greater connectivity to subcortical systems, whereas modern breed dogs exhibit derived expansion and reorganization of cortical circuitry. This dissociation aligns with established allometric scaling principles in mammals: as total brain size increases, the cerebral cortex, particularly association cortex, expands disproportionately relative to subcortical regions (Finlay et al., 2001), and white matter investment increasingly favors long-range cortico-cortical projections over cortico-subcortical pathways (Warling et al., 2021). In our dataset, this shift is associated with increased trainability. Importantly, trainability is best conceptualized as a composite cognitive phenotype rather than a unitary trait (Jones & Gosling, 2005). It likely reflects coordinated variation in learning rate, capacity to form arbitrary cue-response mappings (including vocabulary acquisition) (Helton, 2010), accurate interpretation of human social cues (Wallis et al., 2020), sustained task engagement, working memory, inhibitory control, and social motivation to attend to and cooperate with humans (Serpell & Hsu, 2005).

Many human equivalents of these traits may support our remarkable ability to learn complex behaviors from other humans. For example, the capacity to acquire arbitrary symbol–meaning mappings underlies language learning (Chafe, 1967); working memory and inhibitory control support rule maintenance and flexible updating (Palladino et al., 2001); reading ostensive cues allows for a richer body of information to be learned (Banaji et al., 2013); and sustained social attention and motivation enables shared intentionality, imitation, and cooperative problem solving (Tomasello & Carpenter, 2007). Comparative work suggests that in the hominin lineage, expansion and reorganization of distributed association networks were central to these behavioral shifts (Buckner & Krienen, 2013; Krienen & Buckner, 2020). In humans, these associative regions consist of frontoparietal systems underlying action observation (Hecht et al., 2013), temporoparietal systems involved in social inference (Mars et al., 2013; Saxe & Kanwisher, 2003), and multimodal temporal cortex supporting semantic integration (Ralph et al., 2017). Our findings suggest that selection on trainability in modern breed dogs may represent a parallel elaboration of structural association networks supporting cooperative social learning in humans.

This study has several limitations. The modern breed sample was heavily weighted toward breeds historically bred for work rather than just companionship and was less diverse than the premodern sample. Future work should include a greater variety of modern breeds to ensure that the traits observed in this study are generalizable. Furthermore, although widely used, diffusion-derived FA provides an indirect proxy of microstructure and myelination (Beaulieu, 2002; Ganzetti et al., 2014). This measure cannot fully disambiguate axon density, caliber, and myelin thickness (Warling et al., 2021). Histological validation in future postmortem work would strengthen mechanistic interpretation.

Altogether, our results indicate that strong, behavior-focused artificial selection in the past two centuries has reshaped the canine connectome. Selection for flexible learning of complex skills in a cooperative context has resulted in a transition to more cortex-centric white matter organization. This mirrors key anatomical shifts thought to have occurred in the human lineage (Buckner & Krienen, 2013; Preuss, 2011). Our work is consistent with the view that reorganization of white matter connectivity is a major target of selection for the rapid acquisition of complex, novel behavioral repertoires. It also demonstrates that dogs are a powerful model for understanding the mechanisms of brain-behavior evolution. Even within a single species and a short evolutionary timescale, the wiring of the brain can be substantially reconfigured to meet the demands of a new social and behavioral niche.

Chapter 6 Plastic Adaptations for Skill in the Labrador Retriever Brain

Co-Authors: Isabel Levin, Sonya Ganeshram, Katie Dabney and Erin Hecht

6.1 Abstract

The relative influences of genes and the environment on brain organization are difficult to parse in humans and most model species. Domestic dogs offer a powerful model for dissociating these influences, because selective breeding has produced lineages with heritable predispositions for specific working roles, while the expression of those roles depends on extensive training. We used voxel-based morphometry on T2-weighted structural MRI images from 63 Labrador retrievers drawn from five populations that vary systematically in breeding lineage and training history: hunting dogs and scent

detection dogs belonging to a hunting lineage, service dogs and released service dogs belonging to a service lineage, and companion dogs belonging to a companion lineage. We found evidence of plastic neural adaptations in both the hunting and service lineages. But when we compared the two non-working groups from different lineages, released service dogs and companion dogs, we found no evidence of innate neuroanatomical adaptations in either group. These results suggest that experience-dependent plasticity, rather than breeding lineage, is the dominant force shaping regional brain morphology in Labrador retrievers.

6.2 Introduction

A central challenge of neuroscience is to understand how heritable and experiential factors shape brain organization and function (Krubitzer & Kahn, 2003). This question is especially salient in large-brained species like humans, where prolonged postnatal development and adaptations for plasticity create extensive opportunities for experience to sculpt the brain (Sherwood & Gómez-Robles, 2017). Yet parsing these two influences has been difficult. Studies in humans offer unparalleled access to complex cognition but are constrained by wide variation in genetic background and experience, making causal inference elusive (Brandes et al., 2022; Siddiqi et al., 2022). Rodent models permit precise experimental control but lack the behavioral complexity and developmental timescales relevant to large-brained taxa (Zhang et al., 2023). What is needed is a system that combines the experimental tractability of animal models with the brain complexity and ecological richness found in primates and other large-brained species (Barron et al., 2021).

The domestic dog (*Canis familiaris*) provides exactly this. Centuries of selective breeding for specialized working skills have generated lineages with heritable predispositions for specific learned behaviors—herding, retrieving, and guarding, among others (MacLean et al., 2019). Crucially, these skills are not fully specified at birth but instead depend on extensive training and environmental exposure to be expressed (Hall et al., 2021). Dogs also possess complex brains, extended developmental windows (Bray et al., 2021; Gross et al., 2010), are embedded in human environments, and are amenable to neuroimaging (Thompkins et al., 2016) and behavioral assessment. Together, these features make the

dog an unusually powerful system for asking how inherited neural biases and lived experience jointly shape brain organization.

The Labrador retriever is especially well suited for this purpose. Within this single breed, distinct populations have been selectively bred for different working roles, including hunting and service work, while a large non-working companion population also exists (Lampi et al., 2020; Wiener et al., 2017). Because all Labradors share a common breed-level genetic background, comparisons across these populations reduce the broad genetic variation that typically complicates comparisons across breeds. Importantly, this does not imply that genetic variation is absent within Labradors: genomic analyses have identified measurable within-breed structure associated with working, show, and pet lineages (Wiener et al., 2017). Rather, this structure creates the conditions for a natural experiment in which breed-level ancestry is held relatively constant, while breeding lineage and training history vary systematically.

To exploit this structure, we used structural MRI to compare brain morphology in Labradors from five groups that vary in lineage and training experience. We organized these groups into three breeding lineages: a hunting lineage, from which both hunting dogs and scent detection dogs are drawn; a service lineage, from which trained service dogs and released service dogs are drawn; and a companion lineage, comprising non-working dogs bred for conformation and companionship. The hunting and companion lineages trace back to the field/show split that began in the 1960s, representing approximately 20–30 generations of divergence at a generation interval of 2–3 years. The service lineage derives from breeding programs established in the 1980s, representing approximately 15–20 generations of selective breeding for service-related traits. Released service dogs were dogs that had entered but not completed a professional service dog training program and were released for medical rather than behavioral reasons, meaning they were not removed due to temperamental unsuitability for service work. Critically, both the released service dogs and the companion dogs are non-working family dogs, but they originate from different breeding lineages, with one being selected for service work and the other not. This provides a key contrast for separating the effects of lineage from those of training.

This design enables three specific comparisons aimed at disentangling the relative contributions of selective breeding and training experience to brain organization. First, comparisons between each

actively working group—hunting, scent detection, and service dogs—and released service dogs identify neural features associated with each working role, although these differences may reflect lineage, training history, or their interaction. Second, comparisons among dogs from broadly similar lineages but with different training experiences test whether specific work histories are associated with experience-dependent neural plasticity. Hunting and scent detection dogs share a retriever working-dog background but perform distinct tasks, while service dogs and released service dogs share a service-dog breeding background but differ in current working status. Third, comparisons between non-working dogs from different breeding backgrounds test whether lineage-related differences in brain organization are present in the absence of current professional work. Companion dogs and released service dogs are both non-working at the time of study, but differ in breeding background and early training history, allowing selective breeding and early developmental experience to be evaluated separately from ongoing working demands.

In the current study, we used voxel-based morphometry on T2-weighted structural MRI images of 63 Labradors to investigate whether breeding lineage and training experience are associated with differences in brain morphology. We predicted that each working population would show distinct neural signatures reflecting the sensory and cognitive demands of its role, that specific training histories would drive experience-dependent changes detectable within lineages, and that lineage-based differences would be evident even among dogs without professional training.

6.3 Methods

6.3.1 Ethics Statement

The Institutional Animal Care and Use Committee (IACUC) and Internal Review Board (IRB) of Harvard University reviewed and approved the procedures of this study.

6.3.2 Subjects

All 64 subjects were single breed Labrador Retrievers. The study groups consisted of 12 scent detection dogs, 12 hunting dogs, 17 service dogs, 11 released dogs, and 12 companion dogs. The mean ages were 1.30 ± 0.52 years for scent detection dogs, 3.18 ± 2.44 years for hunting dogs, 1.94 ± 0.76 years for service dogs, 4.43 ± 1.26 years for released service dogs, and 4.00 ± 2.54 years for companion

dogs (Figure 22). Subjects were recruited from working dog institutions and private owners. The service and released dogs came from America's VetDogs service dog population. The service dogs were individuals who were in the final stages of their institutional training, whereas the released service dogs were dogs who were released from the program for non-behavioral reasons to live as pets in private homes. In contrast, the scent detection and hunting dogs were bred for hunting by private breeders. The scent detection dogs were near the end of their institutional training at the Penn Vet Working Dog Center. The hunting dogs belonged to private owners across the United States and were trained by professional dog trainers.

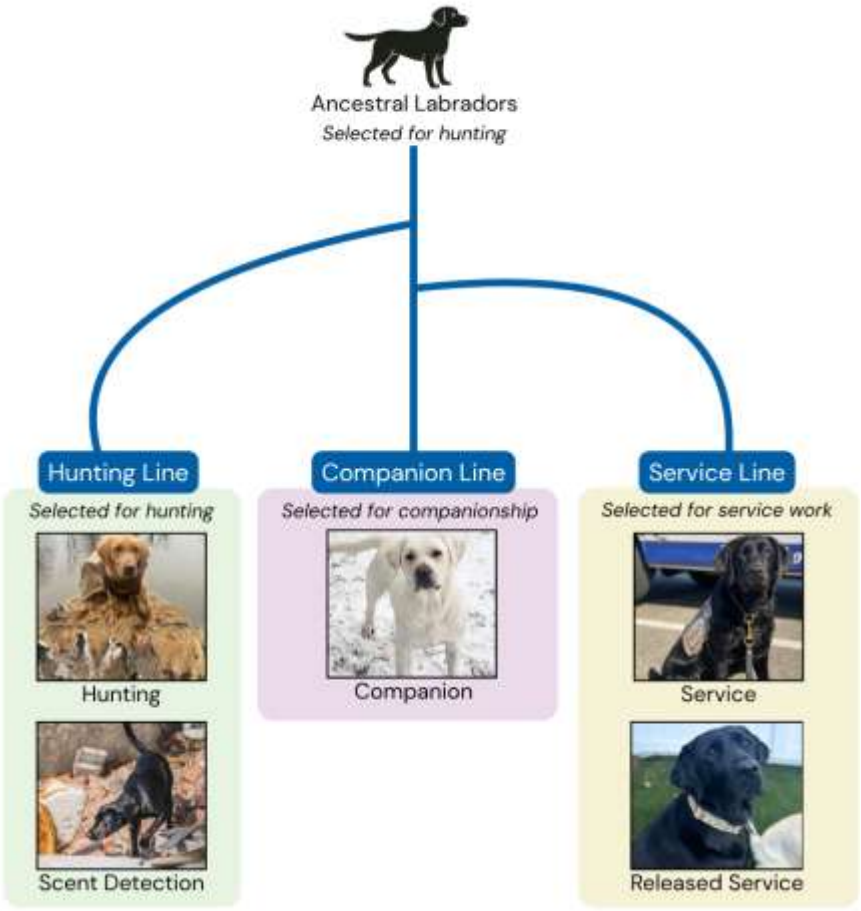


Figure 22. Groups of Labrador retrievers included in the study.

	Subject	Group	Age	Sex
1	Spud	Hunting	1.7	Female intact

2	Jefferson	Hunting	4	Male intact
3	Billy	Hunting	8.8	Male intact
4	Louise	Hunting	2.7	Female desexed
5	Annie	Hunting	2.3	Female intact
6	Paddy	Hunting	2.1	Male intact
7	Maxine	Hunting	1.1	Female intact
8	Boss	Hunting	1.1	Male intact
9	Twister	Hunting	1.1	Male intact
10	Theo	Hunting	2.3	Female intact
11	Jack	Hunting	6.42	Male desexed
12	Buckshot	Hunting	2.58	Male intact
13	Joe	Scent Detection	1.3	Male intact
14	Lambert	Scent Detection	0.8	Male intact
15	Argus	Scent Detection	0.8	Male intact
16	Jesse	Scent Detection	0.9	Male intact
17	Boston	Scent Detection	1.7	Female intact
18	Rio	Scent Detection	0.8	Male intact
19	Vauk	Scent Detection	1.8	Female desexed
20	Marc	Scent Detection	1.25	Male intact
21	Sage	Scent Detection	1.1	Female intact
22	Dude	Scent Detection	1.1	Male intact
23	Villa	Scent Detection	1.58	Female desexed
24	Edgar	Scent Detection	2.5	Male desexed
25	Chichy	Service	3	Female desexed
26	Cue	Service	2.5	Female desexed
27	Paisley	Service	2.3	Female desexed
28	Zucch	Service	1.7	Male desexed
29	Westley	Service	1.2	Male desexed
30	Arbor	Service	2.6	Male desexed
31	Kelly	Service	2.5	Female desexed
32	Harley	Service	1.3	Male desexed
33	Ramses	Service	1.9	Male desexed
34	Tune	Service	2.5	Female desexed
35	Odin	Service	1.7	Male desexed
36	Jojo	Service	0.7	Male desexed
37	PJ	Service	2.5	Male desexed
38	Kelbi	Service	2.6	Male desexed
39	Bloom	Service	2.4	Female desexed
40	Otis	Service	0.7	Male desexed
41	Hope	Service	0.7	Female desexed
42	Max	Released Service	1.8	Male desexed
43	Grey	Released Service	6.2	Male desexed
44	Ryan	Released Service	5.2	Male desexed
45	Coco	Released Service	4	Female desexed
46	Toby	Released Service	5	Male desexed
47	Sally	Released Service	3.7	Female desexed
48	Polka	Released Service	4.4	Female desexed
49	Caroline	Released Service	5.67	Female desexed
50	Daisy	Released Service	4.7	Female desexed
51	Tartan	Released Service	3.8	Male desexed
52	Angel	Released Service	4.3	Female desexed

53	Luna	Companion	3.08	Female desexed
54	Blizzard	Companion	0.58	Female intact
55	Joseph	Companion	2.5	Male desexed
56	Benito	Companion	2.25	Male desexed
57	Nala	Companion	6	Female desexed
58	Lola	Companion	2	Female desexed
59	Lappa	Companion	5.33	Female desexed
60	Maggie	Companion	9.5	Female desexed
61	Jayce	Companion	2.42	Male desexed
62	Poppy	Companion	3.33	Female desexed
63	Hunter	Companion	5	Male desexed
64	Winston	Companion	6	Male desexed

Table 9. Subjects in the dataset. Age is provided in years.

6.3.3 Procedure

Dogs were anesthetized during their MRI scans to avoid potential discomfort and the need for extensive training to lie awake and motionless inside the MRI machine. This anesthetization was performed by a licensed veterinarian familiar with the dog's medical history and health status. The veterinarian sedated dogs with butorphanol and dexmedetomidine (0.3 mg/kg +3 5 mcg/kg, i.m.) and induced general anesthesia using propofol (to effect, 2–6 mg/kg, i.v.), which was maintained with isoflurane O2. While anesthetized, dogs were continuously monitored by the veterinarian and two veterinary technicians using the following parameters: ECG, SpO2, NIBP (oscillometric), and capnography (InVivo Expression MRI-safe unit). T2-weighted structural images (0.667 mm3, 1 average) and 60-direction DWI images (1.30 mm3, 2 averages with reversed phase encoding, 12 B0s) were collected within a ~1 hour scanning session. Afterwards, dogs were recovered from anesthesia while being monitored by a veterinary technician. A bandana and framed image of the dog's brain was given to the dog's owner or handler to take home.

6.3.4 Voxel-Based Morphometry

Regional gray matter morphometry between the five groups was compared using voxel-based morphometry – an approach that analyzes the entire brain in a data-driven manner. The ANTs software package was used in an in-house pipeline to isolate the brain from the images (Avants et al., 2011)

(http://picsl.upenn.edu/software/ants/). A study-specific, symmetric template brain was then made using the software FSL (Jenkinson et al., 2012; Smith et al., 2004) (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki) by registering and merging images from a randomly selected set of 10 dogs from each of the five groups. ANTs was used to non-linearly register the subjects' images to the template (Avants et al., 2011) and the FSL FAST tool was used for bias-field correction and gray matter, white matter, and cerebro-spinal fluid segmentation.

A Jacobian image was generated by multiplying the Jacobian determinant of the ANTs warp field by the gray matter mask for each subject. The Jacobian image shows how each part of the brain had to spatially transform to match the study-study specific average brain template. The five groups were compared in a pairwise fashion using the FSL randomise tool, which does Monte Carlo permutation testing of a general linear model (Winkler et al., 2014). Our significance threshold was set at $p < 0.05$ after family-wise error correction through threshold-free cluster enhancement (Smith & Nichols, 2009).

6.4 Results

There were significant differences in regional gray matter volume across multiple group comparisons (Figure 23, Tables 10–13). Compared to released service dogs, scent detection dogs had significant expansions in parts of the frontal cortex (prorean gyrus, right subprorean gyrus, right anterior composite gyrus), temporal cortex (sylvian gyrus, right anterior ectosylvian gyrus, right mid sylvian gyrus), parietal cortex (presplenial gyrus, right lateral fissure), occipital cortex (right ectolateral gyrus, anterior suprasylvian sulcus, caudal splenial gyrus, splenial sulcus, posterior marginal sulcus, anterior marginal gyrus, and right anterior pararecurrens gyrus), mid cingulate gyrus, and left inferior colliculus. Released service dogs did not show any significantly enlarged regions compared to scent detection dogs.

Relative to released service dogs, hunting dogs showed significantly enlarged parts of the right prorean gyrus, left anterior composite gyrus, and left anterior sylvian gyrus. There were no significantly expanded regions in released service dogs compared to hunting dogs. Compared to released service dogs, service dogs showed significant expansion in parts of the prorean gyrus, pregenual gyrus, and anterior composite gyrus. Released service dogs had an enlarged hippocampus compared to service

dogs. There were no significant differences in regional gray matter volume between companion dogs and released service dogs.

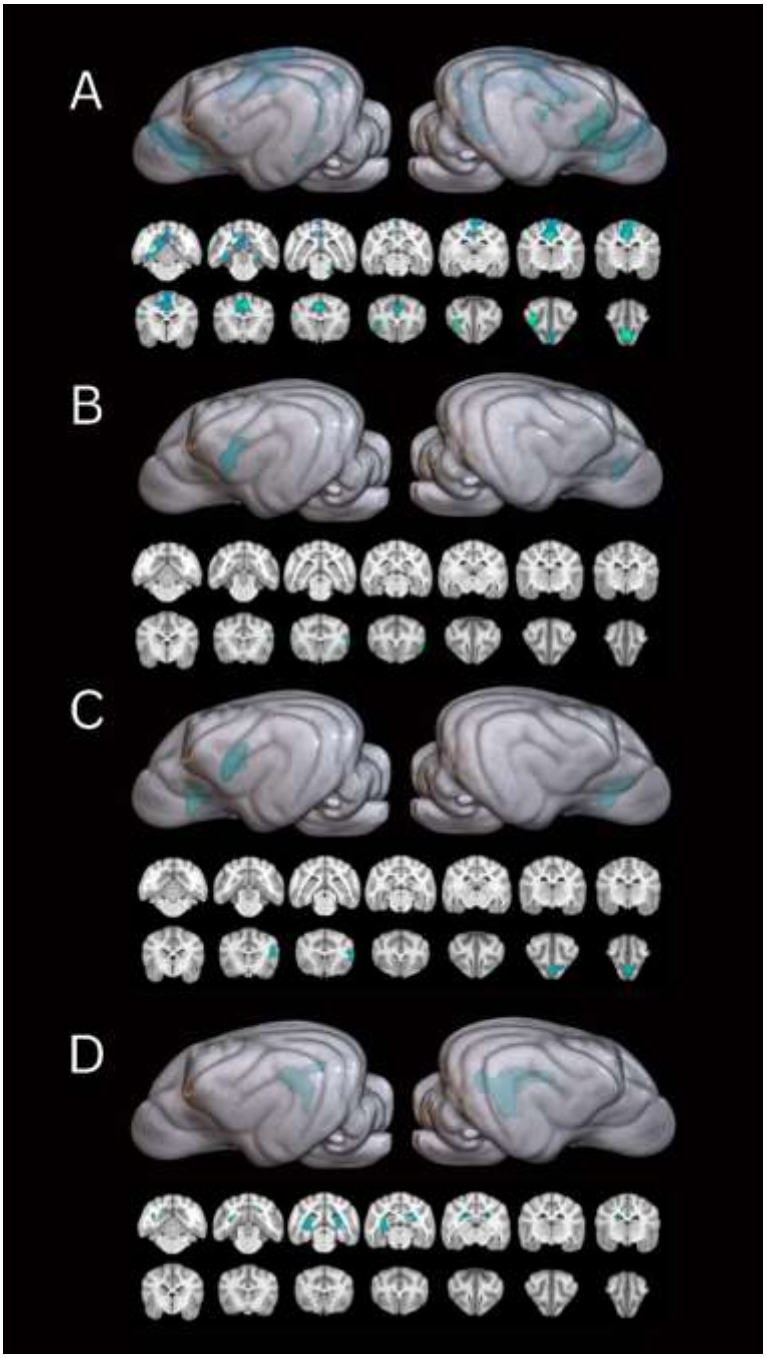


Figure 23. Significantly enlarged regions of gray matter volume in scent detection dogs relative to released service dogs (A), hunting dogs relative to released service dogs (B), service dogs relative to

released service dogs (C), and released service dogs relative to service dogs (D). Colored regions are p < 0.05 after correction for multiple comparisons.

Compared to hunting dogs, scent detection dogs showed expansion in parts of frontal cortex (precruciate gyrus), temporal cortex (left posterior ectosylvian gyrus) parietal cortex (posterior ectolateral gyrus, right ectolateral sulcus, presplenial gyrus, presylvian sulcus, right posterior marginal gyrus, anterior marginal gyrus), occipital cortex (right posterior entolateral gyrus, anterior suprasylvian sulcus, left anterior suprasylvian sulcus, splenial sulcus, suprasplenial sulcus), anterior cingulate gyrus, right posterior cingulate gurus, and cerebellum. Meanwhile, relative to scent detection dogs, hunting dogs showed expansion in the dorsal hippocampus and right caudate (Figure 24, Table 14,7).

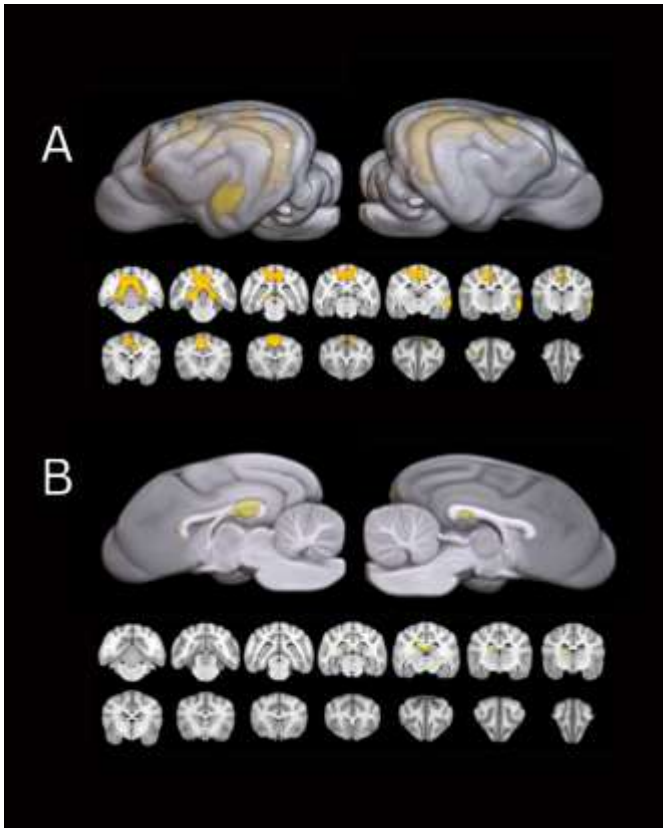


Figure 24. Significantly enlarged regions of gray matter volume in scent detection dogs relative to hunting dogs (A) and hunting dogs relative to scent detection dogs (B). Colored regions are p < 0.05 after correction for multiple comparisons.

Cluster Index	Voxels	Max	Max X (vox)	Max Y (vox)	Max Z (vox)	Cog X (vox)	Cog Y (vox)	Cog Z (vox)
11	17065	65	65	112	74	61.3	97.5	81.1
10	9077	60	60	152	32	60.4	153	34.6
9	8331	40	40	56	46	55	55.1	64
8	3028	38	38	125	47	35.9	133	49.2
7	520	81	81	62	41	80.4	64.6	34.9
6	409	21	21	99	52	26.5	99.2	57.2
5	194	84	84	59	50	85.5	58.3	50.4
4	178	72	72	69	19	75.7	68.6	18.3
3	80	23	23	112	67	22.9	112	66
2	27	103	103	122	46	103	121	45.5
1	9	101	101	120	56	101	120	55.1

Table 10. Information for clusters expanded in scent detection dogs relative to released service dogs depicted in Figure 23A.

Cluster Index	Voxels	Max	Max X (vox)	Max Y (vox)	Max Z (vox)	Cog X (vox)	Cog Y (vox)	Cog Z (vox)
3	1236	6.28	103	121	45	101	118	50
2	1029	6	55	152	38	55.9	153	36.9
1	91	6.59	86	100	47	86	99.2	47.2

Table 11. Information for clusters expanded in hunting dogs relative to released service dogs depicted in Figure 23B.

Cluster Index	Voxels	Max	Max X (vox)	Max Y (vox)	Max Z (vox)	Cog Z (vox)	Cog Y (vox)	Cog Z (vox)
2	3529	5.11	64	140	28	63.6	142	31.7
1	1797	6	96	111	58	98.6	114	54.2

Table 12. Information for clusters expanded in service dogs relative to released service dogs depicted in Figure 23C.

Cluster Index	Voxels	Max	Max X (vox)	Max Y (vox)	Max Z (vox)	Cog X (vox)	Cog Y (vox)	Cog Z (vox)
2	4933	5.41	39	72	45	40	74.5	55.4
1	2727	5.99	81	84	68	80.1	72.6	62.4

Table 13. Information for clusters expanded in released service dogs relative to service dogs depicted in Figure 23D.

Cluster Index	Voxels	MAX	MAX X (vox)	MAX Y (vox)	MAX Z (vox)	COG X (vox)	COG Y (vox)	COG Z (vox)
4	37375	1	88	66	34	60.8	75.7	74.3
3	2856	1	105	97	21	107	87.5	35.9
2	107	1	42	138	54	39.9	138	60.6
1	60	1	78	98	92	78.2	99.7	93.4

Table 14. Information for clusters expanded in scent detection dogs relative to hunting dogs depicted in Figure 24A.

Cluster Index	Voxels	MAX	MAX X (vox)	MAX Y (vox)	MAX Z (vox)	COG X (vox)	COG Y (vox)	COG Z (vox)

2	1846	1	48	95	52	53.4	84	61.6
1	60	1	47	130	45	49.4	130	48.5

Table 15. Information for clusters expanded in hunting dogs relative to scent detection dogs depicted in Figure 24B.

6.5 Discussion

The interplay between inherited neural biases and experience-dependent plasticity remains a central puzzle in neuroscience (Haimson & Mizrahi, 2025). The domestic dog presents a rare natural experiment for dissociating genetic and experiential contributions to brain organization. Working Labrador Retrievers are selectively bred for distinct functional roles, yet the specific environments and training regimes those dogs encounter vary substantially. By comparing regional gray matter volume across five groups of Labradors that differ in genetic background and life experience, we were able to ask whether gray matter organization more closely tracks heritable predispositions or lived experience. Our results suggest that experience-dependent plasticity contributes more to neuroanatomical variation in Labrador retrievers than genetic background.

Compared to released service dogs, all three working groups (service, hunting and scent detection) showed gray matter expansion in the prorean gyrus and the anterior composite gyrus. The prorean gyrus is a prefrontal region involved in executive control (Hecht et al., 2019), whereas the anterior composite gyrus acts as a transitional hub integrating sensory, motor, and motivational processes, with extensive connections to prefrontal cortex (Kosmal et al., 1984). That this expansion was common to all working groups, regardless of the specific skill trained, suggests that it reflects a domain-general neural substrate that indexes the capacity to acquire complex learned behaviors. Thus, while the content of what is learned differs between working roles, the underlying neural infrastructure for learning appears to be shared.

Superimposed on this shared foundation, we observed focal neuroanatomical differences associated with specialized skill training. Relative to released service dogs, scent detection dogs showed

additional gray matter expansion in multisensory cortical regions, association cortex, cingulate gyrus, and inferior colliculus. They also showed expansion in regions of sensorimotor cortex and cerebellum compared to hunting dogs. These findings suggest that the sensory and cognitive systems most relevant to a trained skill undergo domain-specific plastic adaptation shaped by the content of training experience. Hunting dogs, by contrast, showed expansions in the hippocampus and right caudate nucleus relative to scent detection dogs. The hippocampus is broadly implicated in spatial memory and navigation (Eichenbaum, 2017; O'keefe & Nadal, 1978), while the caudate nucleus is involved in goal-directed learning and action (Grahn et al., 2008), functions plausibly engaged by the demands of retrieval work in the field. Together, these results demonstrate that while domain-general prefrontal and premotor regions expand across all working populations, the specific cortical and subcortical territories that differentiate working groups correspond to the particular sensory and cognitive demands of each role.

A notable finding within the service lineage was that released service dogs had a significantly enlarged hippocampus compared to service dogs who completed training. Because these two groups share the same breeding lineage, this difference likely reflects experiential rather than genetic factors. One possibility is that released dogs, having transitioned to life as companion animals in private homes, engage in more autonomous spatial exploration than service dogs, whose movement is closely guided by a handler and constrained by the demands of assistance work. Enriched spatial experience is known to promote hippocampal neurogenesis in rodents and gray matter expansion in humans (Garthe et al., 2016; Maguire et al., 2000). Alternatively, or additionally, the hippocampal difference may relate to chronic stress. Service dogs operate in demanding, highly structured environments that may impose sustained physiological stress, and chronic stress is well established as a driver of hippocampal volume reduction and suppressed neurogenesis (Lee et al., 2009; Mirescu & Gould, 2006). Released service dogs, by contrast, may experience lower baseline stress levels in their role as household pets. These two explanations are not mutually exclusive: greater spatial freedom and reduced stress may jointly contribute to hippocampal expansion in the released population.

Perhaps the most striking finding was the absence of significant morphological differences between companion dogs and released service dogs. These two groups come from distinct breeding

lineages (one selected for conformation and companionship, the other for service work) yet share the common feature of living as non-working companion dogs. Several interpretations of this null result merit consideration.

First, it may be that insufficient evolutionary time has elapsed since the divergence of these lineages for selection to have produced innate neuroanatomical differences in gray matter detectable at the resolution of our methods. Or it could be that there has been sufficient time, but these changes have taken place in other neural traits, such as connectivity or functional activity.

Second, it is possible that companion Labradors are, in a sense, preadapted for the kinds of social and cognitive demands that define service work. As discussed in chapter 3, the Labrador retriever is a modern breed of dog with a highly trainable, expanded cerebral cortex (Barton et al., 2025). The breed's historical development as a hunting retriever (Wiener et al., 2017) may have endowed it with a neuroanatomical profile that already approximates what service work requires. The disproportionate representation of Labrador retrievers in service programs worldwide may thus reflect, at least in part, a pre-existing neuroanatomical suitability for the demands of assistance work

Third, it could be the case that service dog breeding programs unintentionally select for increased neuroplasticity rather than canalization of any particular learned skill. Service dog training demands that dogs acquire a broad and flexible behavioral repertoire such as responding appropriately to unpredictable situations and inhibiting natural impulses in varied social contexts (Bray et al., 2019). Success in such programs may therefore favor brains that are especially responsive to experience, rather than brains that are hardwired for a specific task.

The present findings therefore indicate that, within Labrador retrievers, individual variation in regional gray matter morphology is shaped more strongly by lived experience than by breeding lineage alone. This pattern is consistent with a model in which selective breeding establishes broad behavioral predispositions, but experience and training determine how those predispositions are instantiated in the brain. These findings also have implications relevant to ongoing debates about the nature of hominin cognitive evolution.

Our results suggest that experience plays a larger role than selection in determining within-breed variation in regional gray matter volume. One prominent view holds that the expansion of the human brain involved the elaboration of specialized neural modules for capacities such as tool use and language (Hecht et al., 2015; Rilling et al., 2008). Our data are more consistent with an alternative framework in which selection favored increased neuroplasticity itself rather than the canalization of specific innate abilities. Notably, the Labrador populations in our study do not differ meaningfully in overall brain size, yet they exhibit substantial differences in regional gray matter organization. This suggests that shifts in plasticity can produce marked functional diversification without requiring gross changes in brain volume, a finding that may have parallels in periods of hominin evolution where behavioral complexity appears to have increased without proportional increases in endocranial capacity (Neubauer et al., 2018).

These findings also have immediate practical relevance. Working dogs play critical roles in society as they help disabled people live fuller, safer, healthier lives, locate and rescue survivors of natural disasters, and assist law enforcement and military operations. Yet there are critical shortages of dogs for these roles (Leighton et al., 2018). Training dogs for specialized tasks takes multiple years (Bray, Otto, et al., 2021), costs at least $50,000 per dog (Wirth & Rein, 2008), and fails approximately 50% of the time (Maejima et al., 2007; Slabbert & Odendaal, 1999). Our findings suggest that quantitative neuroanatomical biomarkers, particularly variation in prefrontal and anterior composite gyrus morphology, may offer a biologically grounded basis for predicting working potential. This could lay a foundation for neuroscience-guided improvements to breeding, selection, and training, potentially shifting the field from reactive selection to predictive biology.

Several limitations should be considered. First, the sample sizes for each group in this study were modest, which may have reduced power to detect subtler lineage-based differences. Second, the groups differed somewhat in age and sex composition, which may also contribute to variation in gray matter structure. Third, because this study was cross-sectional, it cannot definitively establish the temporal sequence by which training and environment produced the observed differences. Longitudinal studies following dogs before, during, and after specialized training will be critical for determining how quickly these neuroanatomical changes emerge and whether they persist across the lifespan.

Future work should therefore integrate longitudinal neuroimaging with behavioral and genetic data to test how inherited predispositions interact with training to shape brain development over time. It will also be important to examine whether lineage-based effects are more apparent in other neural phenotypes, such as white matter connectivity or functional network organization, even when gray matter morphometry appears similar. By combining selective breeding history with naturally occurring variation in training experience, dogs provide a powerful model for understanding how genes and experience jointly produce specialized brains.

Chapter 7 Discussion

7.1 Synopsis

Over the course of hominin evolution, the brain was likely a major target of selection, as it underwent an approximately threefold expansion in volume (Holloway et al., 2009). It has long been hypothesized that this expansion was accompanied by substantial alterations to gray and white matter organization, including cortical reorganization, shifts in structural lateralization, and modifications to the connective architecture linking distributed brain regions (Rilling, 2014). Yet our ability to reconstruct these changes is severely constrained by multiple, compounding limitations. Hominin endocrania and endocasts provide only a coarse proxy for brain organization, as external cortical morphology is largely independent of internal neural architecture, rendering features such as regional gray matter variation and white matter connectivity completely invisible to the fossil record (Alatorre Warren et al., 2019). While this can be partially circumvented by investigating the brains of our modern great ape relatives (Rilling, 2014), such comparisons are limited by the long divergence time between great apes and humans (Besenbacher et al., 2019), the possibility that modern ape lineages have themselves diverged considerably from our last common ancestor (Almécija et al., 2021; Staes et al., 2019), and the difficulty of determining which neural differences between humans and apes correspond to which behavioral differences (Logan et al., 2018). The highly plastic nature of the human brain further complicates matters, as it is exceptionally difficult to distinguish innate neural adaptations from specializations that arise

through experience, particularly for socially learned skills such as language and tool use that are universally acquired yet environmentally shaped (Hecht, 2018).

In this dissertation, I have demonstrated how the domestic dog can serve as a living model system to address these challenges and answer major questions relevant to human brain evolution. Dogs offer a uniquely powerful comparative framework because they are a single species in which skull morphology, brain size, behavioral specialization, and selective history vary independently across differentiable, extant lineages — and in which all of these variables can be measured directly using the same neuroimaging methods applied to humans. Critically, the evolutionary history of the domestic dog contains multiple separable phases of selection, from the initial commensal transition, through modest function-driven artificial selection, to the intense selective breeding of the past two centuries (Ritvo, 1986; Wang et al., 2013) that provide a natural comparative design for dissociating variables that cannot be dissociated in the hominin record. Furthermore, the convergent social evolution of dogs and humans, including dogs' orientation toward human social partners (Range & Virányi, 2011) and their capacity to learn from human demonstration (Fugazza & Miklósi, 2014; Topál et al., 2006), makes them especially well-suited for investigating how selection within the anthropogenic niche shapes brain organization.

Across five chapters, I have isolated distinct axes of this variation to test biological principles of brain evolution that are directly relevant to the hominin lineage but otherwise intractable. Chapter 1 examined how regional gray matter volume covaries with skull shape, leveraging the extraordinary range of canine craniofacial morphology to inform how the human brain may have been reorganized as the skull became more globular. Chapter 2 investigated whether structural lateralization in the brain is a consequence of encephalization or a target of selection, exploiting the nearly fourfold variation in brain size across dogs in one of my datasets to partially decouple these two potential drivers. Chapter 3 contrasted modern breed and premodern dogs to test whether selection for social learning from human instructors drives cortical expansion and reorganization of gray matter. Chapter 4 extended this comparison to white matter organization, using diffusion MRI and graph-theoretical analyses to examine how connective architecture responds jointly to scaling and behavioral selection. Finally, Chapter 5 used

within-breed comparisons of working and non-working Labrador retrievers to disentangle inherited neural predispositions from acquired adaptations shaped by occupational experience.

In this concluding chapter, I synthesize the principal findings from each of these investigations, discuss their broader implications for understanding how brains evolve in response to social and ecological pressures, identify limitations of the domestic dog as a model system and of the approaches employed here, and outline directions for future research that could extend and refine this comparative framework

7.2 Chapter Summaries

7.2.1 Chapter 2 Summary

Chapter 2 asked whether variation in skull shape is associated with variation in regional gray matter volume in domestic dogs. Using voxel-based morphometry on T2-weighted MRI images from 79 dogs, I found that neurocephalic index, which is the ratio of neurocranium width to length, significantly predicted gray matter reductions at both extremes of the skull-shape continuum. In dogs with shorter, wider neurocrania (higher neurocephalic indices), reductions were confined to the most rostral and caudal portions of the brain, including the right olfactory bulb, frontal cortex, marginal gyrus, and cerebellum. In dogs with longer, narrower neurocrania (lower neurocephalic indices), reductions were more widespread and encompassed the olfactory bulb, frontal cortex, temporal cortex, amygdala, hypothalamus, hippocampus, periaqueductal gray, cerebellum, and brainstem. No regions showed expansion at either extreme; rather, mesocephalic dogs with intermediate skull shapes had the largest gray matter volumes across the brain.

These results clearly demonstrate that selection on skull shape can alter regional gray matter volume. Therefore, skull shape changes over the course of hominin evolution likely led to gray matter reorganization. This may help explain why skull shape changes appear to accompany the emergence of behavioral modernity in the human archeological record (Neubauer et al., 2018). However, it should be noted that the gray matter alterations that we observed in this study did not match the changes hypothesized to have occurred in humans based on endocasts and endocrania. For example, in the

transition from ancient to anatomically modern humans, there is clear parietal bulging and expansion of the cerebellum (Neubauer et al., 2018). But in brachycephalic dogs that share a globular skull shape with humans, there are only regional reductions, not expansions.

These differences might relate to the considerable phylogenetic divergence between humans and dogs, who last shared a common ancestor 94 million years ago (Kumar et al., 2022). Humans have a dramatically higher ratio of neurocranium to viscerocranium (facial skeleton) because of considerable brain expansion (Pérez-Claros et al., 2015). In dogs, even in the most extreme brachycephalic breeds, the viscerocranium remains a substantial component of total skull volume (Evans & de Lahunta, 2013). This means that although brachycephalic dogs and modern humans share a superficially globular cranial profile, the underlying proportional relationship between brain and face is fundamentally different. Given that brachycephalic dogs showed only regional reductions relative to mesocephalic dogs, it appears that the brachycephalic neurocranium does not increase in volume with globularization, as it does in humans (Neubauer et al., 2009). Instead, globularization in dogs appears to be achieved more by compressing the facial skeleton, which may be why there are no regional gray matter expansions due to constrained neurocranium size.

Humans and brachycephalic dogs also differ in cranial suture morphology. Brachycephalic dogs exhibit significantly greater cranial suture and synchondrosis closure than mesocephalic dogs (Geiger & Haussman, 2016). This premature and extensive fusion constrains the directions in which the skull can grow during development. According to Virchow's law, when premature suture closure occurs, growth of the skull is typically restricted perpendicular to the fused suture and enhanced in a plane parallel to it (Guimarães-Ferreira et al., 2004). In brachycephalic dogs, increased closure of cranial sutures and synchondroses is associated with a characteristically short, broad skull; consistent with Virchow's law, increased fusion of sutures oriented in the coronal plane would be expected to constrain anteroposterior elongation while permitting lateral widening. Critically, the brain of a brachycephalic dog must develop within a vault whose growth trajectories have been altered by suture pathology (Farke et al., 2019). In anatomically modern humans, by contrast, skull globularization is not associated with pathological suture fusion but rather with changes in brain growth trajectories that drive the overlying bone outward,

particularly in the parietal and cerebellar regions (Flaherty et al., 2016; Neubauer et al., 2018). In humans, the brain is, in a sense, shaping the skull, whereas in brachycephalic dogs, the skull may be more so shaping the brain.

The magnitude of skull shape variation is far more extreme in domestic dogs than in humans or other mammals (Evans & de Lahunta, 2013). This greater extremity in dogs may explain why regional gray matter reductions, rather than expansions, predominate at both ends of the canine skull-shape spectrum. Hominin skull shape changes occurred gradually over tens of thousands of years alongside continued brain growth, allowing neural tissue to expand into newly available cranial space (Neubauer et al., 2018). In generational terms, the transition to a globular neurocranium unfolded over roughly 2,400 human generations, given an average generation time of approximately 27 years (Wang et al., 2023). In dogs, by contrast, artificial selection has reshaped the skull over mere centuries, on the order of 100–200 generations. Although modern breed dogs have evolved larger brains (Barton et al., 2025, Chapter 4), the rapid pace of craniofacial change appears to have constrained the regional distribution of gray matter, which may explain why reductions rather than expansions predominate at both ends of the skull-shape spectrum.

Despite these major differences, the findings of this chapter demonstrate that selection on anatomy other than the brain, such as the skull, can have direct influences on brain morphology. This is very important in the context of hominin evolution, as there have been pronounced changes in skull shape over time related to feeding ecology and potentially also sexual selection. The transition to *Homo* involved dramatic reduction in postcanine tooth size and gracilization of the masticatory apparatus (Demes & Creel, 1988; Ledogar et al., 2016) , while middle Pleistocene *Homo sapiens* underwent craniofacial gracilization potentially driven by selection for reduced aggression and increased social tolerance (Cieri et al., 2014). Because the skull is an integrated structure in which the face, cranial base, and braincase are developmentally and functionally linked, selection on any one component is expected to produce correlated changes in the others, including the endocranial space that houses the brain (Lieberman et al., 2000). The present findings from domestic dogs, in which artificial selection on skull

shape has demonstrably reorganized regional gray matter volume, provide empirical proof of concept that such non-neural skeletal selection pressures can propagate to the brain.

There are several limitations to acknowledge and avenues for future research. First, while this study establishes that skull shape predicts regional gray matter volume, it does not establish whether these volumetric differences have functional consequences. There is indirect evidence to suggest they might, however. The right olfactory bulb was among the regions reduced in brachycephalic dogs, and behavioral studies have documented diminished olfactory performance in brachycephalic breeds, as well as altered functional connectivity (Nakaimuki et al., 2025) . However, the relationship between regional gray matter volume and behavioral or cognitive function in dogs remains largely unexplored. Future work pairing structural neuroimaging with standardized behavioral assays would help determine whether the gray matter reductions observed here translate into measurable differences in sensory processing, learning, or temperament.

Second, the brachycephalic dogs in this sample were predominantly small breeds, whose brains may already be subject to strong constraints on absolute size imposed by miniaturization. It is possible that the gray matter reductions reported in this chapter are partly confounded with the effects of small body size, and that the picture might look different in a sample enriched for larger brachycephalic breeds, such as the St. Bernard or Dogue de Bordeaux, where the brain has more absolute space in which to rearrange itself even if the vault is shortened. Future studies should therefore sample across a wider range of body sizes and skull shapes within the brachycephalic category to disentangle the effects of skull shape from those of overall brain scaling.

Third, this study examined only gray matter. White matter tracts, which connect distant brain regions and underpin functional networks, may also be substantially reorganized by skull shape variation. There is precedent for this in domestic cats, where more brachycephalic Persian cats have been shown to possess less white matter compared to more mesocephalic Persian cats (Schmidt et al., 2017). If analogous white matter reductions occur in brachycephalic dogs, the functional implications could be significant. Diffusion weighted imaging in dogs across the skull-shape continuum would be a natural next

step for characterizing the full extent of neuroanatomical reorganization associated with artificial selection on craniofacial form.

7.2.2 Chapter 3 Summary

Chapter 3 asked whether domestic dogs show structural brain asymmetries, whether those asymmetries scale with brain size, and whether they are associated with networks linked to historical selection for breed function. Using voxel-based morphometry and source-based morphometry on T2-weighted MRI images from 62 dogs of 33 breeds, I found widespread gray matter asymmetries spanning cortical and subcortical regions. Leftward asymmetries were present in portions of the temporal cortex (including the sylvian gyrus, sylvian sulcus, and ectosylvian gyrus), the piriform lobe, the amygdala, and much of the cerebellum and brainstem, while rightward asymmetries were observed in frontal regions (including the prorean gyrus and precruciate gyrus), the thalamus, the hypothalamus, the cerebellum, and the brainstem. These asymmetries did not scale with brain size, despite an almost fourfold range in brain volume across the sample. At the network level, asymmetries were present in all six previously identified dog structural brain networks (Hecht et al., 2019), with more cortically dominated networks tending to show greater asymmetry.

Among the most striking findings was the leftward asymmetry of the temporal cortex, particularly in and around the sylvian sulcus, which is the canine analogue of the primate sylvian fissure (Bryant & Preuss, 2018). This pattern parallels a well-established feature of the human brain, where the perisylvian cortex shows robust leftward structural biases that have been linked to language processing (Takao et al., 2011; Gómez-Robles et al., 2016; Maingault et al., 2016; Price, 2012). Interestingly, in dogs, the left rostral and caudal sylvian gyrus show greater activity in response to dog-directed and infant/directed speech than normal adult human speech (Gergely et al., 2023). Additional temporal regions that were expanded in the left hemisphere included the caudal ectosylvian gyrus, implicated in dog processing of word meaning (Boros et al., 2025) and the caudal suprasylvian gyrus, implicated in dog perception of natural speech (Cuaya et al., 2022) . This suggests that asymmetry in the canine temporal lobe may support the processing of human language as it does in humans.

This interpretation is further supported by evidence that dogs and humans may have undergone convergent selection on neural systems involved in language processing. In another paper I coauthored, my colleagues and I identified a canine homolog of the human arcuate fasciculus with an endpoint in the caudal ectosylvian gyrus, and found that this tract is significantly larger in the left hemisphere (Levin et al., 2024). By contrast, the chimpanzee arcuate fasciculus does not show population-level leftward asymmetry (Hecht et al., 2025), suggesting that humans and dogs may have independently evolved enlargement of the left arcuate fasciculus in response to selection for enhanced language-related or communicative processing. Consistent with this interpretation, the size of the canine tract predicted owner-reported receptive vocabulary size in individual dogs (Levin et al., 2024).

The other endpoint of the dog arcuate fasciculus, the precruciate gyrus, showed rightward asymmetry in dogs. Interestingly, the anterior portion of Broca's area in humans, which is potentially homologous to the canine precruciate gyrus, has a larger surface area in the right hemisphere (Kong et al., 2018). This may also be an equivalent adaptation for language processing (Kong et al., 2022) in both species.

Another notable finding from Chapter 2 was that gray matter asymmetries in the dog brain did not scale with brain size. It has been proposed that hemispheric specialization arises as a consequence of increasing brain size, because larger brains face greater interhemispheric conduction delays and thus benefit from lateralized, within-hemisphere processing (Ringo et al., 1994). Yet despite an almost fourfold range in brain volume in the dog sample studied, no relationship between brain size and asymmetry volume was observed. This finding demonstrates that asymmetry can evolve independently to brain size and is consistent with broader comparative evidence that lateralization is widespread even among small-brained vertebrates and invertebrates (Güntürkün et al., 2020; Rogers et al., 2013), a pattern that is difficult to reconcile with any purely size-dependent account. In the context of human evolution, this means that it cannot be necessarily assumed that observed asymmetries came about through concerted increases in brain volume. An important caveat, however, is that dog brains are considerably smaller than human brains, so it remains possible that scaling effects on asymmetry only emerge above a certain size threshold. The present data cannot rule out such a threshold model.

Chapter 2 further showed that asymmetry was present in structural brain networks that have evolved to support historical breed functions. Asymmetry was more prominent in the networks that were more cortically based, such as the networks for social interaction and drive and reward. This pattern is intriguing because it suggests that lateralization may be especially characteristic of higher-order cortical circuits involved in complex, learned behaviors. Language is strongly left-lateralized (Frost, 1999) as is tool use and skilled manual action (Lewis, 2006; Randerath et al., 2010). The finding that dog brain networks linked to complex working behaviors show greater asymmetry than those involved in basic threat responses thus parallels the broader pattern in humans, where lateralization appears to be the most pronounced in cortical systems that have been shaped by selection on skilled behavior (Ocklenburg & Güntürkün, 2017). This convergence across two distantly related lineages raises the possibility that selection for complex behavioral specializations may preferentially drive the lateralization of cortical networks.

Several limitations of these findings should be acknowledged. Most importantly, the functional relevance of the structural asymmetries reported here remain unknown. While structural asymmetries are often interpreted as reflecting underlying functional lateralization, there need not be a one-to-one correspondence between the two. That said, there is evidence across multiple species that structural asymmetries can be associated with cognitive and behavioral phenotypes (Rogers et al., 2013). For example, in human children, lateralization of the arcuate fasciculus (Qiu et al., 2011) and superior longitudinal fasciculus (J. Liu et al., 2019) is significantly predictive of language abilities. In human adults, the volume of the left arcuate fasciculus is significantly associated with functional language lateralization as measured through a dichotic listening task (Ocklenburg et al., 2014). Meanwhile, in chimpanzees, right handedness is significantly associated with increased leftward lateralization of the planum temporale (Hopkins & Nir, 2010). Future research should therefore investigate the functional correlations of cognition and behavior and structural asymmetries in dogs. It would be particularly informative to further examine how structural asymmetry relates to language processing in dogs to see if there is convergence with what is observed in humans. It would also be interesting to directly test how asymmetry relates to working performance in dogs.

Another limitation of this study was that only gray matter morphology was investigated. However, previous work suggests that certain gray matter asymmetries can be accompanied by parallel asymmetries in white matter (Takao et al., 2011). It is therefore reasonable to expect that given the widespread lateralization of gray matter volume in the canine brain, there would also be considerable white matter asymmetries. Future work should leverage diffusion tensor imaging in dogs to explore potential white matter lateralization.

A final limitation is that the present study examined structural asymmetry at a single time point, making it impossible to determine whether the observed asymmetries are stable traits or whether they fluctuate across development or in response to experience. Longitudinal data would be needed to establish whether these asymmetries are established early in life and remain fixed, or whether they are shaped by training, environmental enrichment, or other experiential factors.

7.2.3 Chapter 4 Summary

Chapter 4 asked whether modern breed dogs and premodern dogs differ in regional gray matter volume, whether those differences mirror the effects of brain scaling, and whether they are associated with variation in trainability and fear. Using voxel-based morphometry on T2-weighted MRI images from 85 dogs (72 modern breed and 13 premodern), I found that modern breed dogs show significant and widespread cortical expansion spanning frontal, temporal, parietal, occipital, and cingulate regions, while premodern dogs show significantly larger subcortical structures, most notably the amygdala, hippocampus, and nucleus accumbens, as well as portions of the hypothalamus and thalamus. A whole-brain analysis of brain size and regional gray matter volume revealed that these modern/premodern differences closely mirror the effects of brain scaling, with increasing brain size associated with cortical expansion and subcortical contraction in the same regions. Cortical expansion significantly predicted individual trainability scores, while amygdala expansion significantly predicted fear scores, including overall fear, stranger-directed fear, dog-directed fear, and nonsocial fear. Modern breed dogs were also rated as significantly more trainable and less fearful than premodern dogs.

Individual dog behavior ratings were obtained from the Canine Behavioral Assessment & Research Questionnaire (C-BARQ) (Duffy & Serpell, 2012; Hsu & Serpell, 2003), which was filled out by

the dogs' owners. In this scale, trainability is conceptualized as a dog's ability to follow human cues, pay attention to humans, learn quickly, and resist distractions during training (Serpell & Hsu, 2005). Many of these component abilities have human equivalents that underpin our own capacity for social learning. The ability to acquire arbitrary symbol-meaning mappings is foundational to language learning (Chafe, 1967), reading ostensive cues from a demonstrator enriches the body of information available to be learned (Csibra & Gergely, 2009), and sustained social attention and motivation enable shared intentionality, imitation, and cooperative problem solving (Tomasello & Carpenter, 2007). Trainability, in this view, can serve as a useful proxy for human-directed social learning ability, and the association between cortical expansion and trainability in modern breed dogs may thus point toward a broader principle, that selection for the ability to learn from social partners can drive expansion of the cerebral cortex.

This idea aligns with, but is more specific than, the social brain hypothesis, which posits that the cognitive demands of navigating complex social environments have been a primary driver of brain enlargement in primates (Dunbar, 1998). The social brain hypothesis focuses on social group size and the computational demands of tracking social relationships, but the dog data suggest that a more targeted selective pressure, the ability to learn complex behaviors from a social partner, may be sufficient on its own to initiate cortical expansion. This is consistent with the cultural brain hypothesis (Muthukrishna et al., 2018), which proposes that selection for the ability to acquire, store, and transmit cultural knowledge can drive brain enlargement independently of group size per se. In dogs, the relevant cultural knowledge is interspecific rather than intraspecific, as modern breed dogs have been selected to learn from human teachers rather than from conspecifics, and recent behavioral evidence suggests that more cooperative breeds preferentially learn from humans over other dogs (Dobos & Pongrácz, 2024; Pongrácz & Dobos, 2025). The fact that cortical expansion predicts trainability at the individual level, within a sample that includes both working and companion dogs, suggests that this relationship is not simply a product of experiential enrichment. It is also supported by a prior study from our lab that found a significant association between breed-average trainability scores and cortical expansion (Hecht et al., 2021), a result that was blind to individual variation in experience and driven entirely by heritable, breed-level traits.

A further consideration is the role of brain scaling in producing these differences. Although a phylogenetic analysis of covariance did not reveal a significant difference in relative brain size between modern breed and premodern dogs, a separate whole-brain voxel-based morphometry analysis showed that variation in total brain size accounts for nearly all of the variation in regional gray matter anatomy observed between the two groups. Increasing brain size was associated with cortical expansion and subcortical contraction in the same regions that distinguished modern breed from premodern dogs. This pattern is consistent with the "late equals large" hypothesis, which holds that as brains scale larger, late-developing structures like the cortex expand disproportionately while earlier-developing structures like the amygdala shrink in relative terms (Finlay et al., 2001). If selection for trainability has favored dogs with larger brains, then the widespread cortical expansion and subcortical reduction observed in modern breeds may be largely a downstream consequence of concerted developmental scaling, rather than the result of independent, mosaic changes to many individual brain regions. If this reasoning is correct, it suggests that selection for social learning ability in hominin evolution may have triggered an increase in brain size that then produced a cascade of correlated neural changes through the predictable logic of allometric scaling.

The premodern side of the equation is also informative, although its relevance to human evolution is less direct. Premodern dogs showed significantly larger subcortical structures, most markedly the amygdala, and amygdala expansion significantly predicted fear scores across multiple C-BARQ subscales. The amygdala processes both positive and negative environmental stimuli and is best known for its role in fear learning (Janak & Tye, 2015). However, fear may not be the only functional domain relevant to amygdala expansion in premodern dogs. The central nucleus of the amygdala has been identified as a modular command system for predatory hunting in rodents, coordinating both prey pursuit, via projections to the periaqueductal gray, and the delivery of killing bites, via projections to the parvocellular reticular formation (Han et al., 2017). This is notable because premodern dogs have strong historical ties to hunting. Many ancient breeds were maintained specifically for hunting purposes. Village dogs and New Guinea singing dogs also hunt prey rather than relying solely on human-provisioned food (Boyko & Boyko, 2014; Ritchie et al., 2013; Surbakti et al., 2020). The enlarged amygdala in premodern dogs may therefore reflect not only heightened fear processing but also the preservation of predatory

circuitry that supports active hunting. These two functions are not mutually exclusive, as both fear-related vigilance and predatory motivation would have been adaptive for dogs living more independently from humans, where survival depended on the ability to detect threats and capture prey.

Modern breed dogs, by contrast, have evolved to be deeply integrated into human society, where survival requires reduced fearfulness and where food is provisioned rather than hunted. Humans may also have directly selected against fight-or-flight and predatory behaviors in modern breeds, particularly in working dogs where such behaviors can conflict with work goals. Notably, portions of the hypothalamus, which is centrally involved in fight-or-flight processing, were also reduced in modern breed dogs. This dual pattern of cortical expansion linked to trainability and amygdala reduction linked to decreased fear and possibly decreased predatory drive is remarkably consistent with neural changes observed in domesticated rabbits (Brusini et al., 2018) suggesting that similar selective pressures may produce convergent patterns of brain reorganization across domesticated species. Together, these findings challenge the long-standing view that domestication consistently involves reductions in brain size and cognitive capacity (Kruska, 1988). Rather, they suggest that the second phase of dog domestication has involved both increases in cortical volume and decreases in subcortical structures involved in fear and predation, a pattern consistent with a dual-phase model of domestication in which early attenuation to the human socio-ecological niche is followed by additional adaptive changes supporting behavioral specialization for particular contexts within that niche (Tancredi & Cardinali, 2023).

This study has several limitations that should be acknowledged. The premodern dog sample was small (n = 13), reflecting the inherent difficulty of obtaining MRI data from village dogs, ancient breeds, and other premodern populations. Phylogenetic analyses were underpowered due to limited genomic data for many of the premodern breeds in the sample, and future work would benefit from genome sequencing of these populations. Behavioral scores were owner-reported, which introduces potential inaccuracy, although the significant correlations between owner-reported behavior and brain anatomy provide some reassurance that the C-BARQ is capturing meaningful variation. Additionally, only gray matter was examined in this chapter, leaving open the question of whether modern breed and premodern dogs also differ in white matter organization, which Chapter 5 addresses directly. Finally, because some

of the modern breed dogs in the sample were enrolled in working dog training programs, it remains possible that experiential differences between modern and premodern dogs account for a portion of the observed neuroanatomical variation. However, the convergence with prior breed-level analyses (Hecht et al., 2021a) and the presence of brain-behavior associations in both working and nonworking individuals argues against a purely experiential explanation. Future work should pair brain imaging with direct behavioral experiments measuring learning speed from human instructors and should aim to recruit a broader sample of premodern dogs, in order to more precisely test the hypothesis that selection on social learning ability is sufficient to drive cortical expansion and the cascade of neural changes that accompany it.

7.2.4 Chapter 5 Summary

Chapter 5 asked whether the gray matter differences between modern breed and premodern dogs documented in Chapter 3 are accompanied by corresponding differences in white matter organization, and whether those white matter differences are likewise associated with trainability. Using tract-based spatial statistics (TBSS) and whole-brain probabilistic tractography with graph-theoretical analyses on diffusion-weighted MRI from 52 dogs (29 modern breed and 23 premodern), I found that modern breed dogs exhibit significantly greater fractional anisotropy (FA) across large, distributed clusters spanning cerebral white matter as well as thalamic and midbrain regions, with no regions showing greater FA in premodern dogs. FA within these modern-enriched clusters positively predicted individual C-BARQ trainability scores. At the network level, modern breed dogs exhibited reduced weighted clustering coefficients, distinct community organization including an independent cerebellar-collicular module not found in premodern dogs, and increased cortical hub prominence, particularly in frontal and parietal regions. Premodern dogs, by contrast, showed greater relative subcortical connectivity and unique subcortical hubs. Together, these findings indicate that recent artificial selection for trainability is associated with large-scale reorganization of the canine connectome, and that even over short evolutionary timescales within a single species (roughly 80 generations), selection on behavior can substantially reshape structural brain connectivity.

These white matter findings complement and extend the gray matter results of Chapter 4 in several ways that are relevant to understanding brain evolution. Perhaps most importantly, the network analyses revealed that larger-brained modern breed dogs have a more modular connectome than smaller-brained premodern dogs, with eight network communities compared to seven in premodern dogs. This shift toward greater modularity with increasing brain size is consistent with established scaling principles in comparative neuroscience, as the connectome becomes progressively more modular as brain volume increases (Puxeddu et al., 2024). As brains grow larger, total white matter volume increases but scales sublinearly relative to the expansion of the cerebral cortex (Ardesch et al., 2022), imposing constraints on long-range connectivity that favor the development of (more segregated, locally clustered network architectures. A similar process likely occurred during hominin brain evolution, as the threefold increase in brain size from early australopiths to modern humans would have been accompanied by predictable shifts in network organization, with long-range connections becoming relatively sparser and the brain becoming increasingly partitioned into functionally specialized modules.

One particularly striking feature of the modularity results is the emergence in modern breed dogs of a distinct cerebellar-collicular community that is not segregated as an independent module in premodern dogs. In premodern dogs, the cerebellum, superior colliculus, and inferior colliculus are integrated into other network communities, whereas in modern dogs these structures form their own separate module. This suggests that the cerebellum becomes more functionally independent as brain size increases, which has direct relevance to hypotheses about cerebellar involvement in hominin cognitive evolution. The human cerebellum expanded and became more rounded during the evolution of anatomically modern *Homo sapiens* (Neubauer et al., 2009), and there is growing recognition that the cerebellum contributes to cognitive functions well beyond motor coordination, including language, working memory, and social cognition (Stoodley & Schmahmann, 2018). The dog data suggest that increased cerebellar independence from the rest of the connectome may be a predictable consequence of brain scaling, and that this reorganization may have created new computational possibilities as the hominin brain enlarged.

The FA findings provide further insight into how white matter microstructure changes with brain scaling and selection. Modern breed dogs showed significantly greater FA across widespread cerebral white matter, with no regions showing greater FA in premodern dogs. Greater FA is commonly interpreted as reflecting increased axonal coherence, packing density, and myelination (Beaulieu, 2002). Myelination is energetically efficient for maintaining connectivity speed across the longer distances that characterize larger brains (Wang et al., 2008), and it is implicated in skill learning and performance in both humans and other animals (Hecht, Pargeter, et al., 2023; Shimizu et al., 2023; Xin & Chan, 2020). These myelination differences may mean that dogs (and by analogy, hominins) with larger, more heavily myelinated brains may have been better equipped from the outset to learn complex behaviors efficiently. The fact that FA within modern-enriched clusters was significantly and positively correlated with individual trainability scores reinforces this interpretation, linking white matter microstructure directly to the ability to learn from humans.

At the nodal level, the connectivity analyses revealed that regions showing the greatest increases in weighted degree in premodern dogs were predominantly subcortical, including the cerebellum, superior colliculus, inferior colliculus, and geniculate nuclei. Modern breed dogs, by contrast, showed the greatest connectivity increases in cortical regions, particularly frontal areas including the pregenual and prorean gyri, as well as parietal and sensorimotor cortex. The anterior composite gyrus, a frontal region that acts as a transitional hub integrating sensory, motor, and motivational processes (Kosmal et al., 1984), was also highly connected and expanded in larger brains, and warrants further investigation as a potentially important node in the reorganization of the canine connectome under selection for trainability. These nodal results converge with the Chapter 4 gray matter findings and with the broader argument of this dissertation, that selection for social learning drives a reallocation of neural resources from subcortical to cortical systems, and that this shift is accompanied by corresponding changes in structural connectivity.

This chapter has several strengths compared to Chapter 4. The sample was larger (52 dogs compared to 85 in Chapter 3, but with a substantially more balanced group composition of 29 modern breed and 23 premodern dogs, compared to 72 and 13), and the premodern sample was more diverse, including village dogs from multiple continents as well as a wider range of ancient breeds. The

convergence between the white matter results reported here and the gray matter results of Chapter 4 strengthens the overall argument that modern breed and premodern dogs differ systematically in brain organization, and that these differences are associated with trainability. The use of three complementary analytical approaches, TBSS and graph-theoretical network analysis, provides converging evidence from different levels of white matter organization.

The study also has limitations. The modern breed sample was heavily weighted toward breeds historically bred for work rather than companionship and was less diverse than the premodern sample. If working dogs specifically, rather than modern breeds as a whole, prove to have relatively larger brains, this would strengthen rather than undermine the social learning hypothesis, as it would indicate that the lineages subject to the most intensive selection for acquiring behaviors from human instructors exhibit the greatest degree of neural divergence. Nonetheless, future work should include a broader range of modern breeds to determine how generalizable these findings are. Additionally, the cross-sectional design of this study cannot determine the extent to which the observed white matter differences reflect heritable variation versus experience-dependent plasticity, although both modern breed and premodern dogs lived in human households, with some undergoing training for sports or work. Future research should investigate how global white matter architecture changes with scaling and selection in greater detail, ideally in longitudinal designs that can track the development of these connectivity patterns over time.

7.2.5 Chapter 6 Summary

Chapters 3 and 4 established that modern breed and premodern dogs differ substantially in both gray and white matter organization, but those comparisons alone cannot reveal the source of the differences—whether they reflect evolved, heritable traits or experience-dependent plasticity. To investigate the potential roles of heritable adaptations and acquired plastic change in canine brain organization, I used voxel-based morphometry on T2-weighted MRI images from 63 Labrador retrievers drawn from five groups that vary systematically in breeding lineage and training experience: hunting dogs and scent detection dogs from a hunting breeding lineage, service dogs and released service dogs from a service breeding lineage, and companion dogs bred for companionship and/or conformation. This within-breed design holds broad genetic variation roughly constant while allowing breeding lineage and

occupational experience to vary independently. I found that all three working groups (hunting, scent detection, and service dogs) showed gray matter expansion in the prorean gyrus and anterior composite gyrus relative to released service dogs, suggesting a shared, domain-general neural substrate for the acquisition of complex learned behaviors. Superimposed on this shared foundation, each working group showed focal expansions in regions plausibly related to its specific training demands, with scent detection dogs showing the most widespread differences, including expansion of multisensory cortex, association cortex, cingulate gyrus, and cerebellum, and hunting dogs showing expansion in the hippocampus and caudate nucleus. Critically, non-working companion dogs and released service dogs, who share the experience of living as household pets but come from different breeding lineages, did not differ significantly in regional gray matter volume. This pattern of results suggests that, within a single modern breed, experience-dependent plasticity contributes more to neuroanatomical variation than breeding lineage alone, and that over the short evolutionary timescales separating these lineages (approximately 20–30 generations for the hunting/companion split dating to the 1960s, and 15–20 generations for the service lineage dating to the 1980s), selection may have favored increased neuroplasticity rather than canalized, hardwired specialization for particular skills.

The most striking finding of Chapter 5, and the one with the clearest implications for understanding human brain evolution, is that neuroanatomical variation within Labrador retrievers appears to be shaped more by lived experience than by breeding lineage. The critical comparison is between released service dogs and companion dogs, two groups that share the experience of living as non-working household pets but come from different breeding lineages (one selected for service work, the other for conformation and companionship). Despite their distinct selective histories, these two groups did not differ significantly in regional gray matter volume. By contrast, dogs that differed in training experience but came from the same lineage, such as service dogs versus released service dogs, or hunting dogs versus scent detection dogs, showed significant neuroanatomical differences. This pattern indicates that, over the relatively short evolutionary timescale separating these breeding lineages, selection has not produced detectable canalized differences in gray matter morphology. Instead, the brain appears to rely on experience-dependent plasticity to produce the neural specializations associated with particular working roles.

This result must be reconciled with the findings of Chapters 4 and 5, which documented substantial and likely heritable brain differences between modern breed and premodern dogs. The key distinction is timescale. Modern breed dogs are the product of approximately two centuries of intense artificial selection (Worboys et al., 2018), representing roughly 65–100 generations of directed breeding. Over this interval, selection has had sufficient time to produce heritable changes in both gray matter (Chapter 4) and white matter (Chapter 5) organization, including widespread cortical expansion, subcortical contraction, increased fractional anisotropy, and altered network topology. Within the Labrador retriever, however, the divergence between hunting and service lineages spans a much shorter period, on the order of 15–30 generations, and involves selection on more specific behavioral phenotypes rather than broad cognitive traits like trainability. Over this shorter timescale, it appears that selection has favored brains that are highly responsive to experience rather than brains that are hardwired for any particular skill. Service dogs are an especially informative case in this regard, because they perform jobs that are historically novel, with no deep selection history for the specific tasks they are trained to do. The fact that service dogs show the same prefrontal expansion as hunting dogs, a group with a far longer selection history for its working role, suggests that this prefrontal signature reflects the general demands of learning complex behaviors from humans, rather than the canalization of any specific skill set.

Superimposed on this domain-general prefrontal foundation, the scent detection and hunting groups showed focal expansions in cortical regions that are plausibly related to the specific sensory and cognitive demands of their trained roles. This suggests that the neural architecture for skilled behavior in dogs consists of two tiers. There is a shared, domain-general infrastructure centered on prefrontal and frontal association cortex that supports the general capacity to learn from humans, and on top of this, domain-specific plastic adaptations emerge in the cortical regions most relevant to a particular skill. This two-tiered architecture has a parallel in the human literature on skill learning. Paleolithic stone toolmaking training produces structural remodeling in frontoparietal regions and neural changes associated with one type of toolmaking generalized to improved performance on a different, untrained toolmaking task (Hecht, Pargeter, et al., 2023). This suggests that selection for one complex skill can produce neural substrates that transfer to the acquisition of other skills, a principle that the dog data supports, given that all three working groups share a common prefrontal expansion despite being trained for entirely different tasks.

Among the three working groups, scent detection dogs showed the most widespread neuroanatomical differences relative to released service dogs, with expansions spanning multisensory cortex, association cortex, cingulate gyrus, inferior colliculus, and cerebellum. This may reflect the particular intensity and diversity of scent detection training programs, which require dogs to discriminate among many different target odors, search across varied environments, and sustain focus over extended periods. Furthermore, they receive fitness cross-training, which may further shape their brains. The breadth of cortical regions affected in scent detection dogs is consistent with the interpretation that more demanding and multifaceted training regimes produce more extensive experience-dependent plasticity.

Although speculative, these findings may be interpreted in light of a longstanding theoretical framework in evolutionary biology known as the Baldwin effect (Baldwin, 1896). The Baldwin effect proposes that behaviors initially acquired through individual learning can, over evolutionary time, become genetically canalized if the same learning challenge persists across generations (Sznajder et al., 2012). In the early phase of this process, individuals succeed through plasticity alone, and selection favors those who learn most readily. If the selective environment remains stable, a later phase may involve the genetic canalization of initially plastic traits, such that behaviors that once required extensive learning become more readily or automatically expressed (Baldwin, 1896). The pattern observed in service dogs, where plastic neural changes associated with skilled performance are present but no canalized lineage-specific differences are detectable, may represent the early phase of this process. Service dogs have been bred for their current role for only a few decades, which may be insufficient time for canalization to have occurred. By contrast, the heritable brain differences between modern breed and premodern dogs documented in Chapters 4 and 5 may represent a more advanced phase of the Baldwin effect, in which traits that were initially acquired through learning have become at least partially canalized over centuries of sustained selection. Dogs in novel working roles, such as service dogs, therapy dogs, and medical detection dogs, are ideal subjects for investigating this process longitudinally, as they allow researchers to observe in real time how the brain responds to new behavioral demands before canalization has had the opportunity to occur.

More broadly, Chapter 6 demonstrates that dogs are a valuable model for studying the interplay between inherited and acquired neural adaptations, a question that is exceptionally difficult to address in humans. In our own species, prolonged postnatal development and extensive adaptations for plasticity make it nearly impossible to determine which aspects of brain organization are genetically specified and which are sculpted by experience (Sherwood & Gómez-Robles, 2017). The dog system, in which breeding lineage and training experience can be partially dissociated within a single breed, offers a tractable alternative for investigating these questions. The present results suggest that, at least over short evolutionary timescales, selection for complex skilled behavior favors increased neuroplasticity rather than the canalization of specific innate abilities. This is consistent with a model of hominin cognitive evolution in which the expansion of the human brain created a more plastic neural substrate that was then shaped by culturally transmitted learning environments, rather than one in which each cognitive capacity evolved its own dedicated neural module.

This chapter has several limitations. Only gray matter was examined, and future work should apply the white matter methods used in Chapter 4 to this within-breed design to determine whether connectivity patterns also track training experience more closely than breeding lineage. Resting-state functional connectivity would be a particularly valuable complement, especially for the companion and released service dog comparison, where no structural gray matter differences were found. Functional differences between these groups could reveal lineage-related variation in neural organization that is not apparent at the level of regional gray matter volume. The cross-sectional design cannot establish the temporal sequence by which training produced the observed differences, and longitudinal studies following dogs before, during, and after specialized training will be important for understanding how quickly these neuroanatomical changes emerge and whether they persist. Future work should integrate longitudinal neuroimaging with behavioral testing and genetic data to more precisely characterize how inherited predispositions interact with training to shape brain development over time, and should investigate whether the expanded cortical regions identified here are predictive of actual task performance. Dogs in novel working roles, where selection histories are short and behavioral demands are well characterized, offer a particularly promising avenue for tracking how the Baldwin effect unfolds in a living system.

7.3 Conclusions, Limitations, and Future Directions

Viewed as a whole, the five chapters of this dissertation demonstrate that the domestic dog is an especially informative model system for investigating principles of brain evolution that are directly relevant to the hominin lineage but otherwise inaccessible. Chapter 2 established that selection on skull shape can reorganize regional gray matter volume, providing proof of concept that non-neural skeletal selection pressures, such as those operating on facial and cranial morphology during hominin evolution, can propagate to the brain. Chapter 3 demonstrated that structural lateralization in the dog brain is widespread but does not scale with brain size, suggesting that hemispheric specialization can evolve independently of encephalization and may instead be linked to selection for complex, skilled behaviors. Chapters 4 and 5 provided convergent gray matter and white matter evidence that selection for social learning ability (trainability) is associated with cortical expansion, subcortical contraction, increased myelination, and large-scale reorganization of the connectome, supporting the hypothesis that selection on the ability to learn from social partners can drive the kind of concerted brain reorganization observed in the hominin fossil record. Chapter 6 showed that, within a single breed over shorter evolutionary timescales, experience-dependent plasticity rather than genetic canalization accounts for the neuroanatomical differences between dogs trained for different working roles, suggesting that selection may initially favor increased neuroplasticity, with canalization of specific traits emerging only after sustained directional selection over longer periods. Across all five chapters, the regions most consistently implicated in behavioral differences were cortical, and prefrontal regions in particular emerged as a recurring locus of both heritable and plastic adaptation, reinforcing the centrality of cortical association areas in the evolution of complex, socially learned behaviors.

Despite the strengths of the domestic dog as a comparative model, several overarching limitations of this dissertation should be acknowledged. First, and perhaps most importantly, this dissertation does not include genetic data. Throughout Chapters 4, 5, and 6, I have drawn inferences about heritability and selection based on comparisons between lineages with different selective histories, but without direct genomic information, these inferences remain indirect. I have collected genetic samples from many of the dogs in these studies, and incorporating genomic data in future analyses will be an

important step toward identifying specific genetic variants associated with the neuroanatomical and behavioral traits described here, quantifying the heritability of these traits more precisely, and testing for signatures of selection at the molecular level.

Second, domestic dogs are phylogenetically distant from humans, with a last common ancestor approximately 94 million years ago (Kumar et al., 2022). While this distance is part of what makes convergent findings between dogs and humans so striking, it also means that homologies between canine and human brain regions are sometimes uncertain, and that similar behavioral phenotypes may be supported by partially different neural mechanisms in the two species. Furthermore, dogs evolved to interact with heterospecific social partners (humans) rather than conspecifics, and this difference in the social context of learning may affect brain-behavior relationships in ways that limit direct translation to the hominin case. That said, the fact that selection for learning from social partners produces cortical expansion in dogs just as it appears to have done in the hominin lineage suggests that there are general principles at work that transcend the specific phylogenetic context in which they operate.

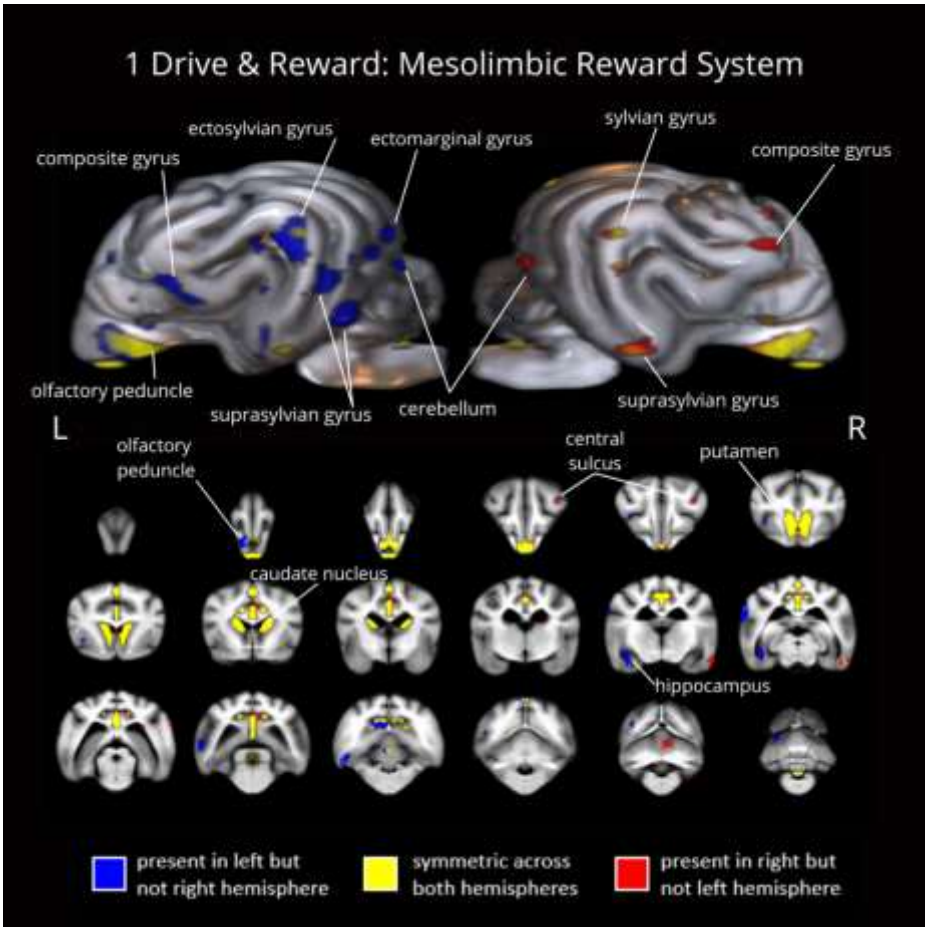
Third, the data analyzed in Chapters 1 and 2 came from an opportunistic sample of dogs who had been referred to a veterinary teaching hospital for suspected neurological issues but were subsequently not diagnosed with a neurological disorder. While these dogs were cleared of gross neurological pathology, it remains possible that subclinical abnormalities could have influenced the results. In future work, I plan to replicate and extend these analyses using the large, high-quality dataset of neurologically healthy dogs that I have since collected at Harvard, which would provide a stronger foundation for the skull-brain and asymmetry findings.

Fourth, the behavioral data used in Chapters 3 and 5 were derived from owner-reported questionnaires (C-BARQ), which are subject to the biases and limitations inherent in any subjective rating system. Owners may overestimate or underestimate their dogs' abilities, and the ecological validity of questionnaire-based behavioral phenotyping remains an open question. The significant correlations between owner-reported behavior and brain anatomy observed in Chapters 3 and 4 provide some reassurance that the C-BARQ is capturing meaningful variation, but future work should supplement owner reports with direct behavioral testing, including standardized assessments of learning speed, social

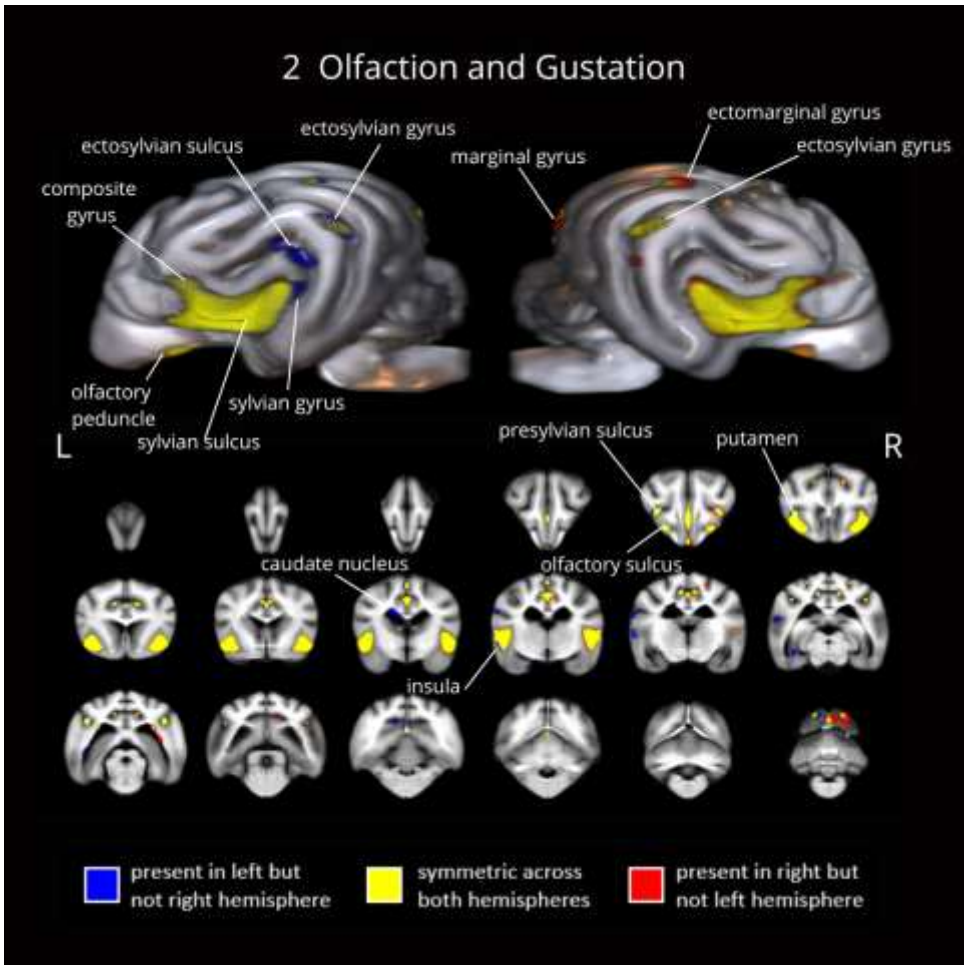
responsiveness, and task performance, to more rigorously characterize the behavioral phenotypes associated with neuroanatomical variation.

Fifth, although each chapter of this dissertation isolates a different axis of variation, the studies are cross-sectional in design and therefore cannot establish causal or temporal relationships between the variables examined. Longitudinal studies that track brain development before, during, and after training would be invaluable for determining how quickly experience-dependent changes emerge, whether they persist after training ceases, and whether heritable differences become more apparent at certain developmental stages.

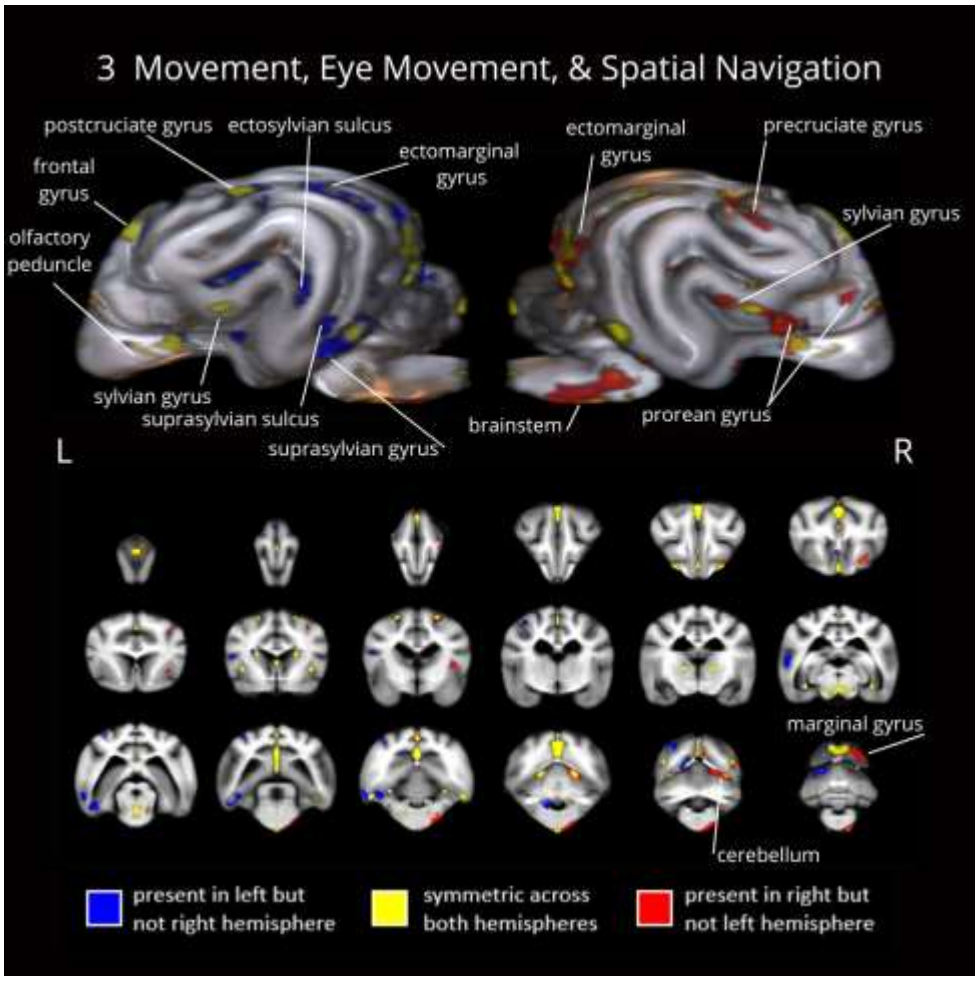
Looking forward, several directions for future research emerge from this work. The most immediate priority is the integration of genomic data with neuroimaging and behavioral phenotyping. Genome-wide association studies and polygenic score analyses, applied to the dogs in these datasets, could identify genetic loci associated with cortical expansion, trainability, and other traits of interest, and could test whether the same genetic variants that distinguish modern breed from premodern dogs also contribute to within-breed variation in brain organization and behavior. Future work should also extend the within-breed design of Chapter 6 to other breeds so that heritable adaptations can be studied in more depth. Some particularly promising candidate breeds include German Shepherds, which have distinct protection, herding, and assistance lineages, and Border Collies, whose working populations have diverged into herding and agility lineages. Finally, the comparative framework developed in this dissertation could be extended to other domesticated species. Horses, for example, have been selectively bred into distinct populations for racing, dressage, draft work, and other roles, each involving different behavioral demands and different training regimes, and equine neuroimaging infrastructure is increasingly available (Johnson et al., 2019). Such extensions would test whether the principles identified here, such as the link between social learning and cortical expansion, the two-tiered architecture of domain-general and domain-specific neural plasticity, and the role of brain scaling in producing cascading neural changes, are general features of how mammalian brains evolve in response to selection on behavior or whether they are specific to the canine case.



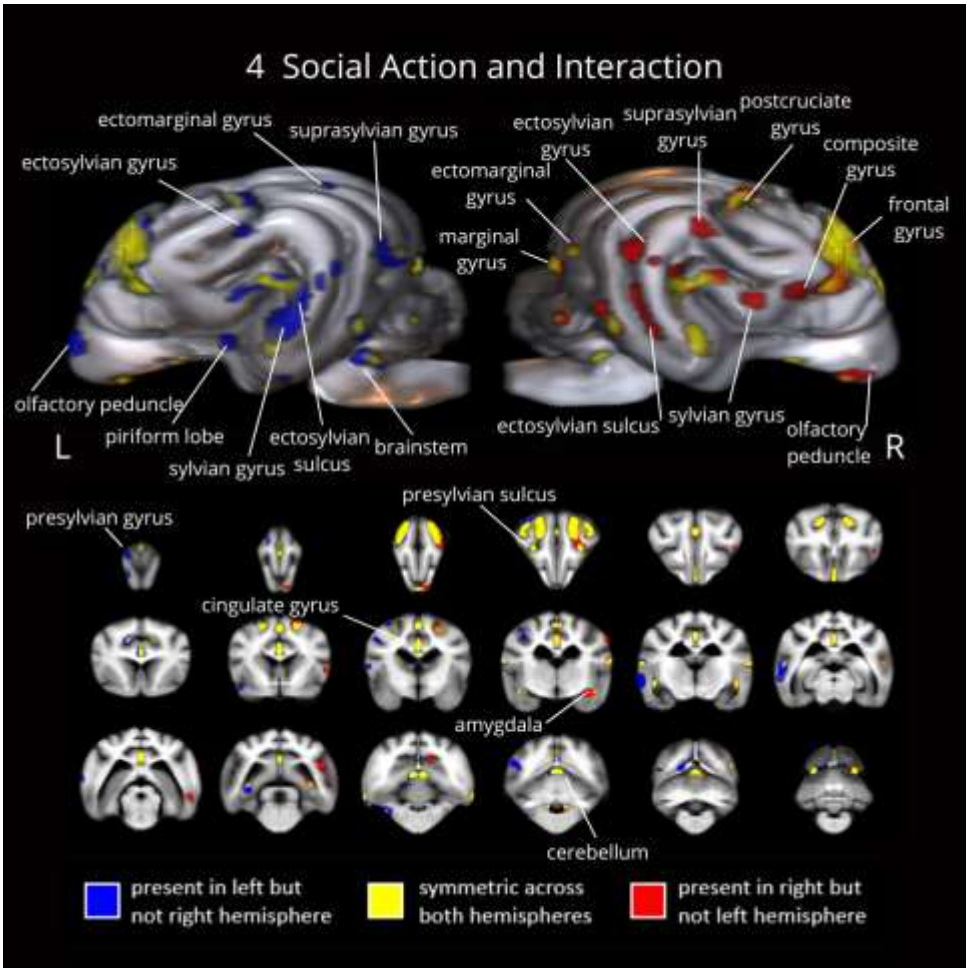
Supplemental Figure 25. Asymmetrical regions of gray matter volume in domestic dogs in network 1, previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



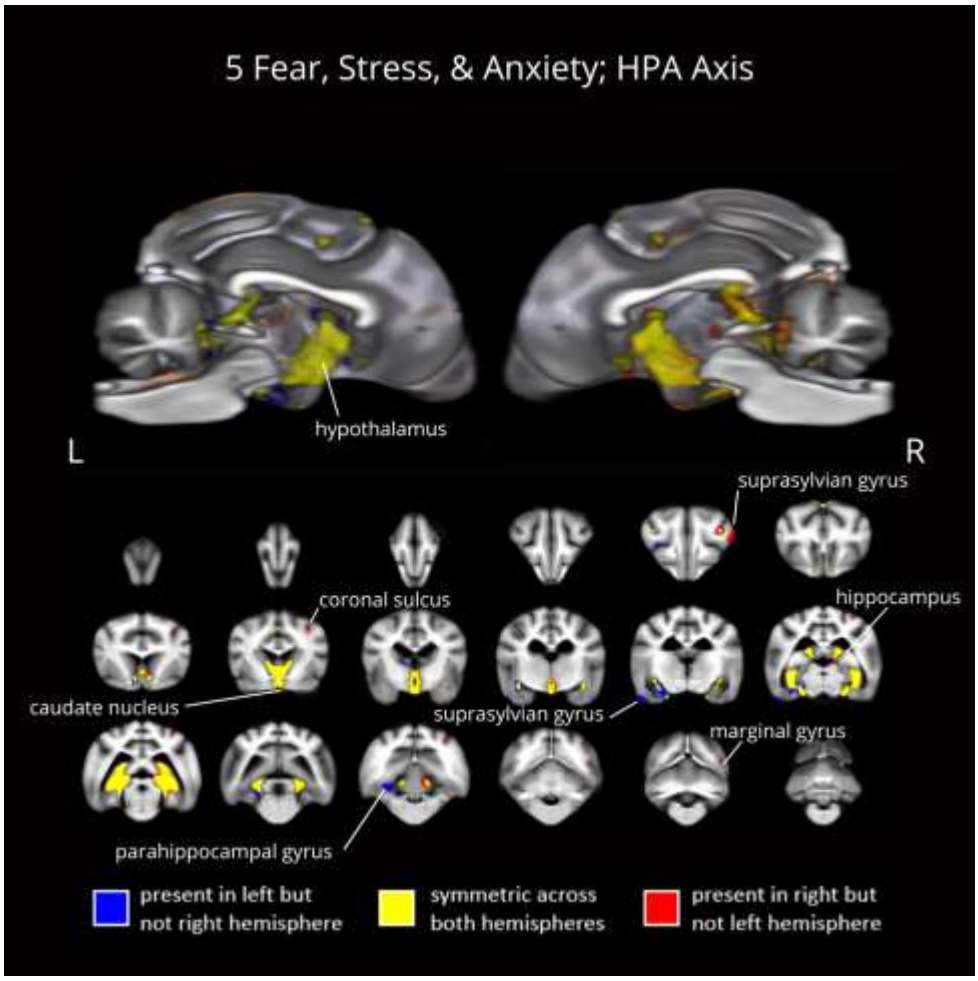
Supplemental Figure 26. Asymmetrical regions of gray matter volume in domestic dogs in network 2, which was previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



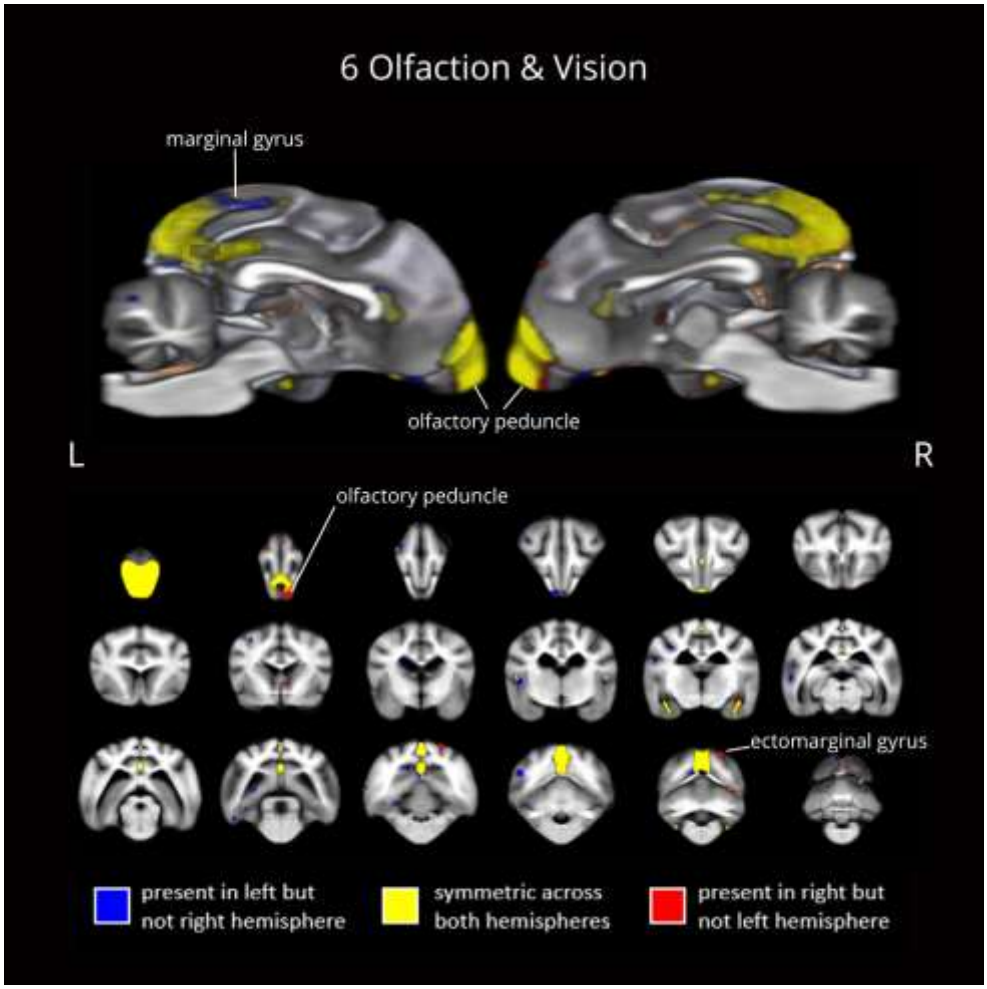
Supplemental Figure 27. Asymmetrical regions of gray matter volume in domestic dogs in network 3, previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



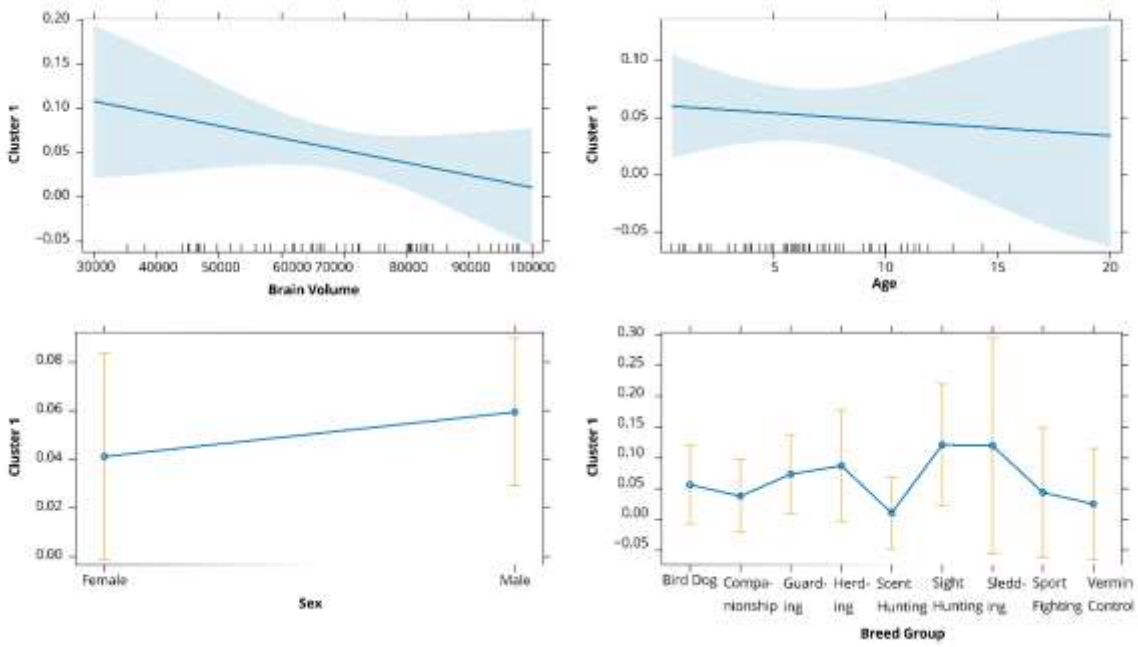
Supplemental Figure 28. Asymmetrical regions of gray matter volume in domestic dogs in network 4, previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



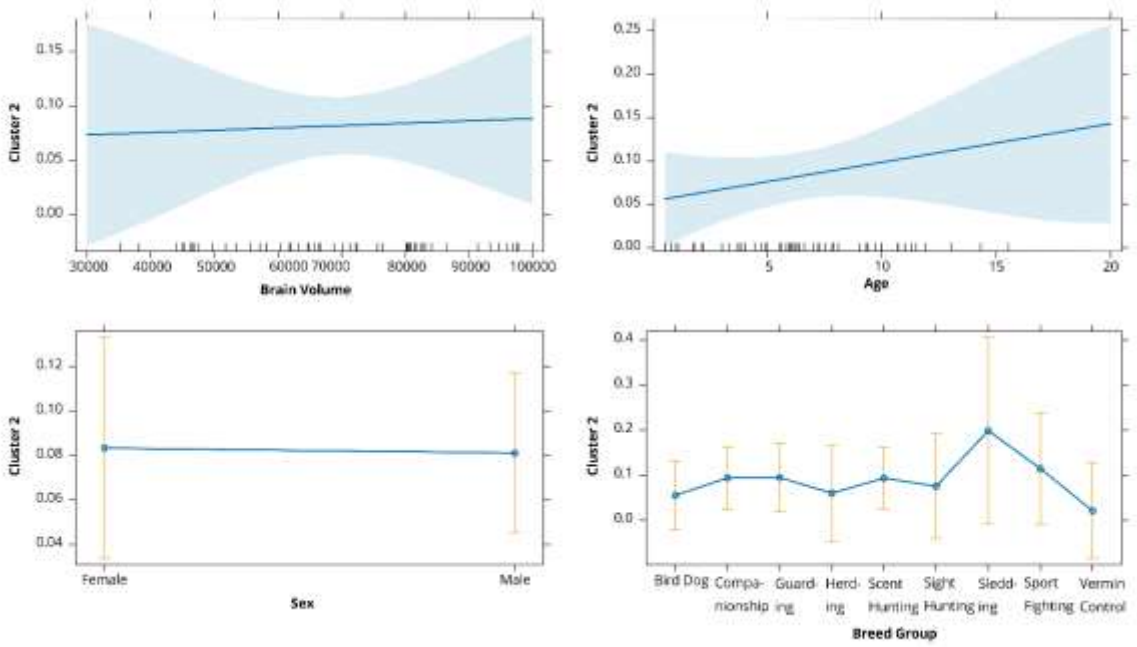
Supplemental Figure 29. Asymmetrical regions of gray matter volume in domestic dogs in network 5, previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



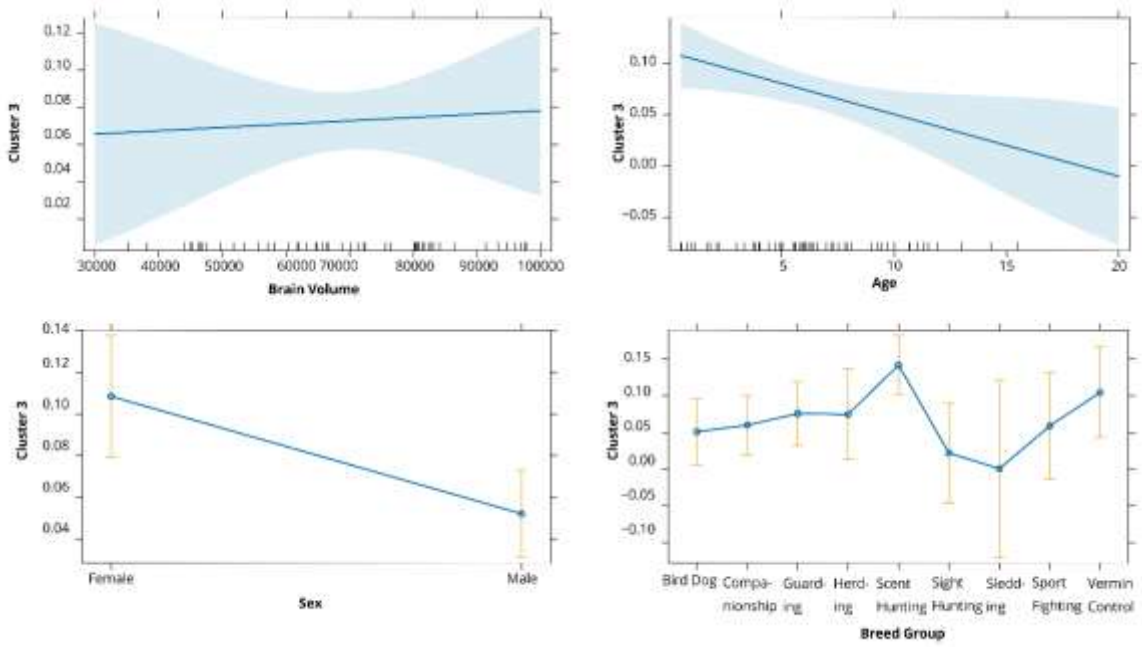
Supplemental Figure 30. Asymmetrical regions of gray matter volume in domestic dogs in network 6, previously identified by Hecht and colleagues (2019). Regions in blue are present in the left but not the right hemisphere. Regions in red are present in the right but not the left hemisphere. Regions in yellow are symmetric across both hemispheres. Asymmetrical regions are all $p < 0.05$ after correction for multiple comparisons.



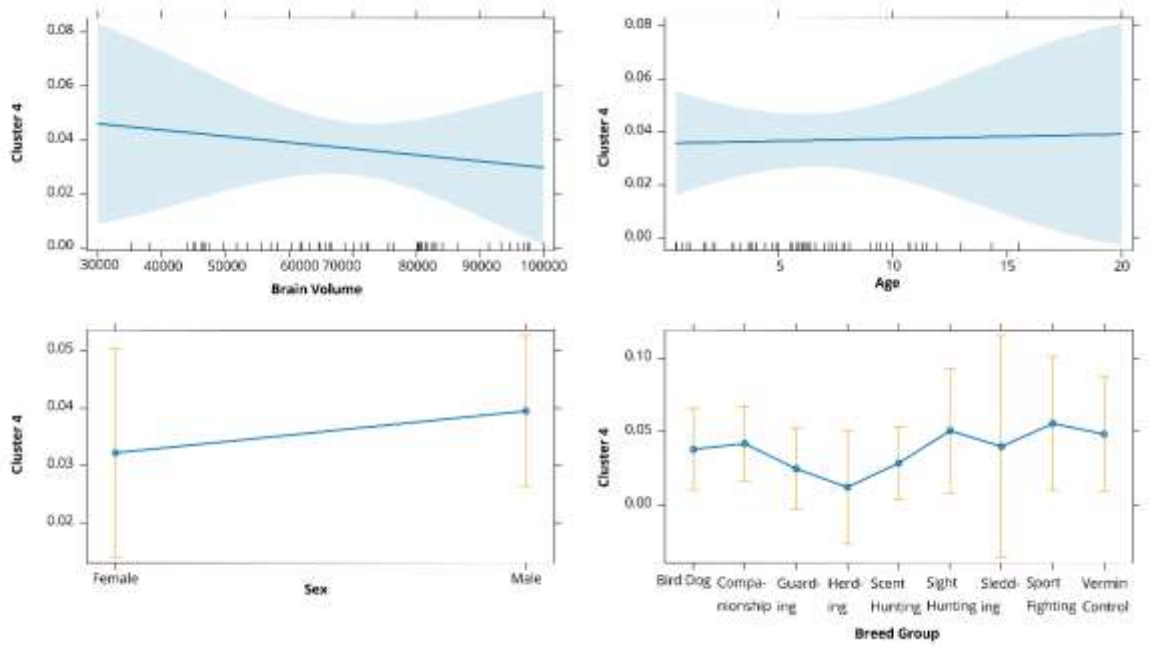
Supplemental Figure 31. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 1.



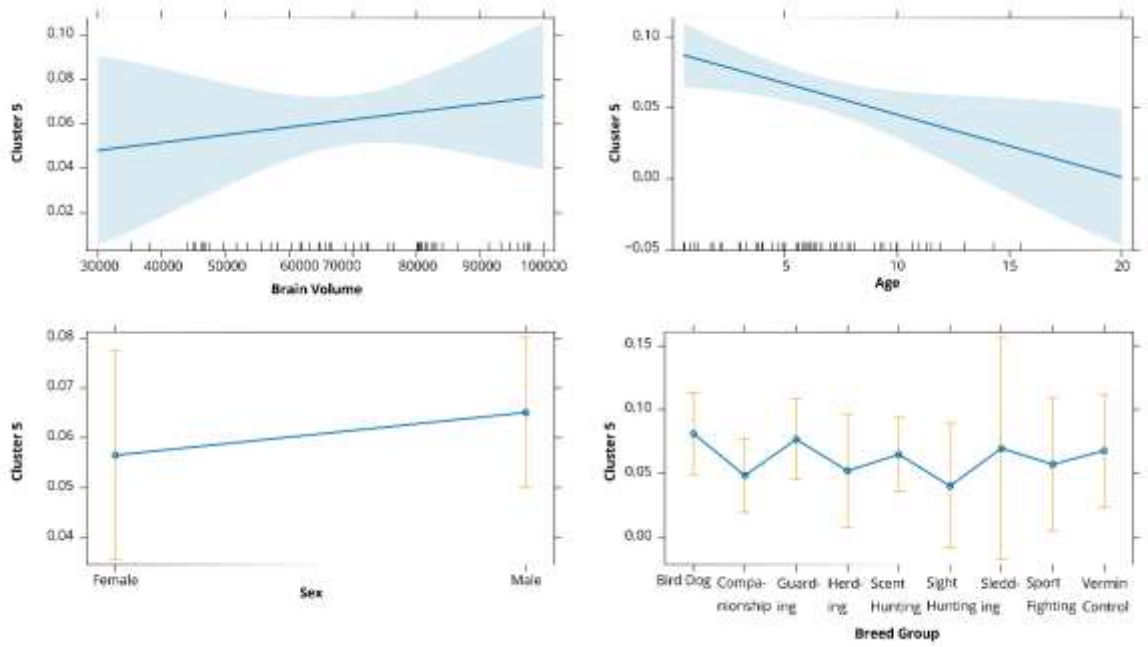
Supplemental Figure 32. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 2.



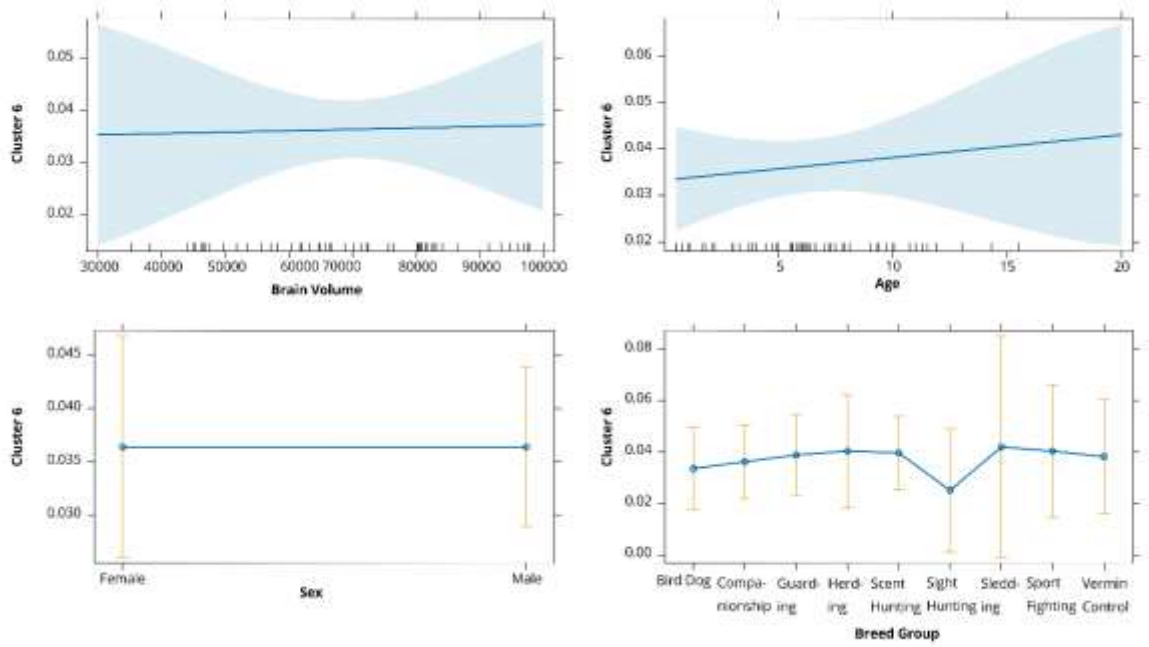
Supplemental Figure 33. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 3.



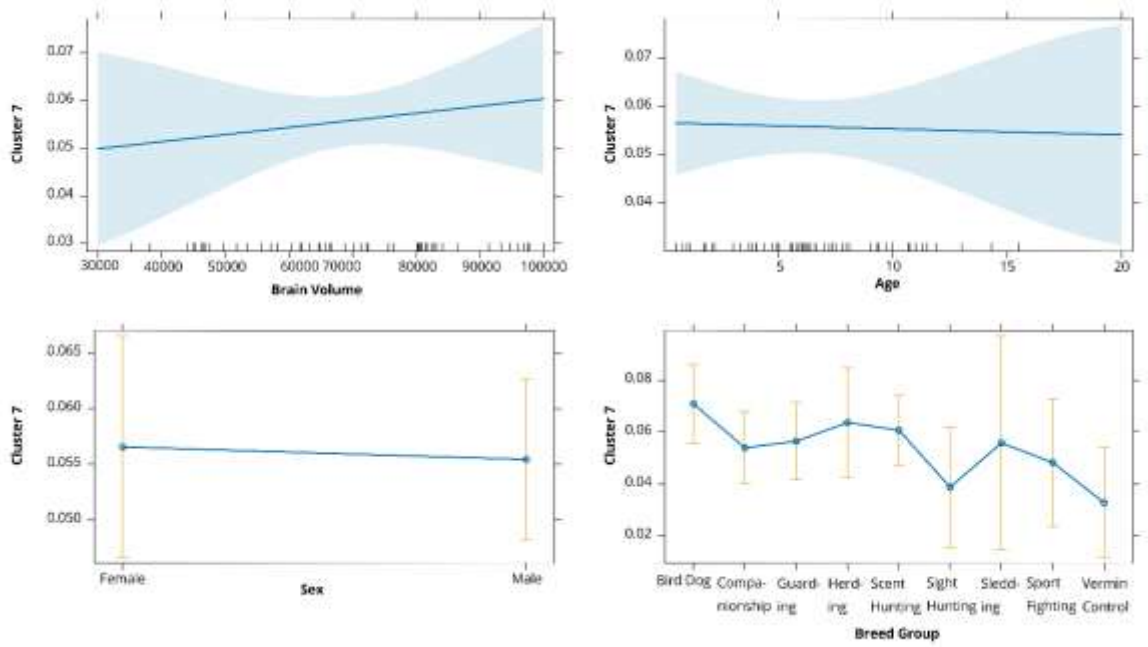
Supplemental Figure 34. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 4.



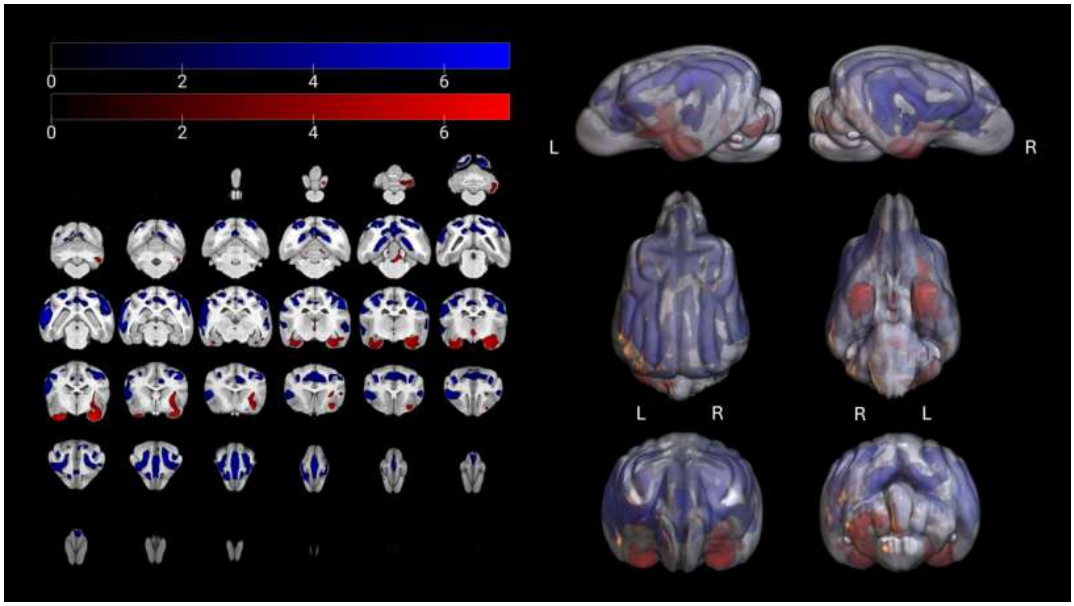
Supplemental Figure 35. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 5.



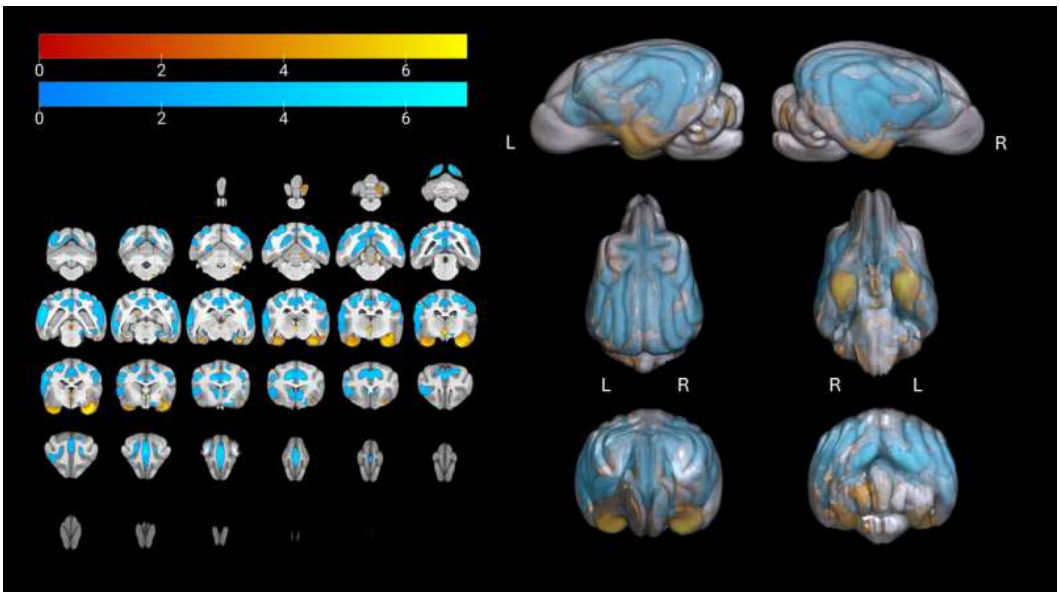
Supplemental Figure 36. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 6.



Supplemental Figure 37. Effects plots for the generalized linear model created to test the effects of brain volume, age, sex, and breed group on the asymmetry of cluster 7.

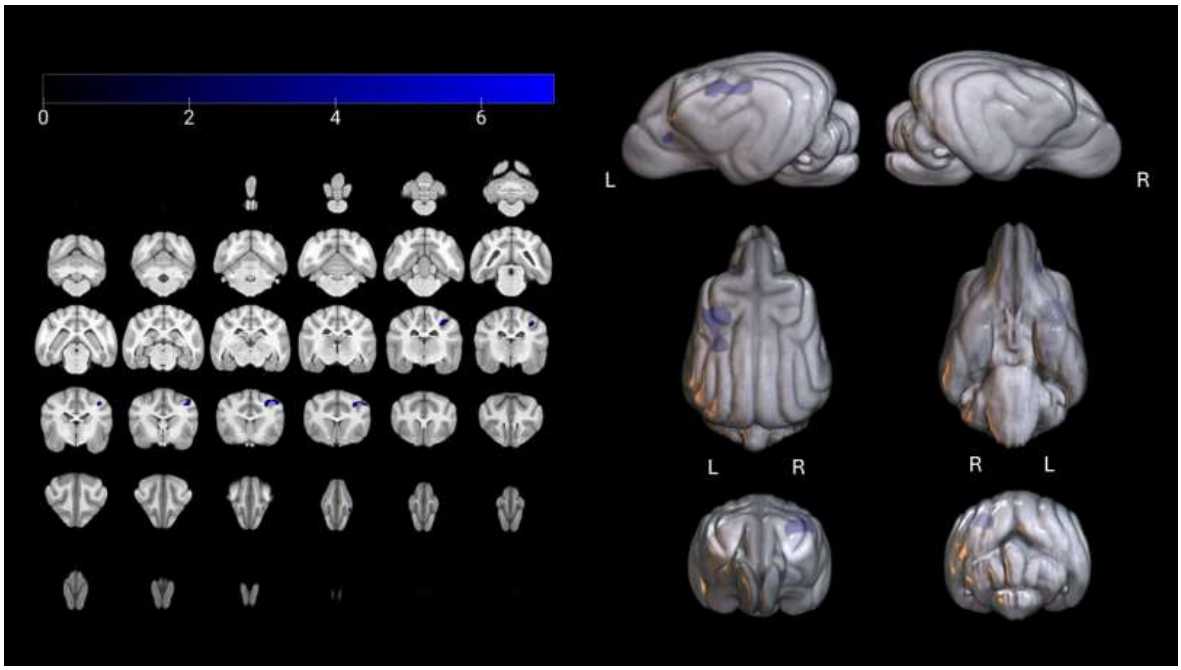


Supplemental Figure 38. Significantly enlarge regions of gray matter volume in modern breed dogs compared to premodern dogs (blue) and significantly enlarged regions of gray matter volume in premodern compared to modern breed dogs (red). Colored regions are all $p < 0.05$ after correction for multiple comparisons; t-statistic values are illustrated. Results displayed on the canine brain atlas created by Johnson et al. (2020).



Supplemental Figure 39. Brain regions that are significantly and positively associated with brain size (light blue) and significantly and negatively associated with brain size (orange). Colored regions

are all p < 0.05 after correction for multiple comparisons; t-statistic values are illustrated. Results displayed on the canine brain atlas created by Johnson et al. (2020).



Supplemental Figure 40. Significantly enlarged brain regions in modern breed dogs compared to premodern dogs, after controlling for brain weight. Colored regions are all p < 0.05 after correction for multiple comparisons; t-statistic values are illustrated. Results displayed on the canine brain atlas created by Johnson et al. (2020).

#	Name	Ancestry	Breed/Type	Sex	Age	Working or Sporting Activities
1	Jack	Modern Breed	Labrador Retriever	Male	6.4	Hunting Fowl
2	Dima	Modern Breed	Border Collie	Female	2.3	None
3	Sophie	Modern Breed	Border Collie	Female	2.4	Herding Livestock
4	Raven	Pre-Modern	West Siberian Laika	Female	2	Barn Hunt
5	Louise	Modern Breed	Labrador Retriever	Female	3.8	Hunting Fowl
6	Hope	Modern Breed	Labrador Retriever	Female	0.6	Service Work

7	Jojo	Modern Breed	Labrador Retriever	Female	0.6	Service Work
8	Pochacco	Pre-Modern	Samoyed	Male	3.6	Rally, Barn Hunt
9	Otis	Modern Breed	Labrador Retriever	Male	0.6	Service Work
10	Harley	Modern Breed	Labrador Retriever	Male	1.3	Service Work
11	Westley	Modern Breed	Labrador Retriever	Male	1.3	Service Work
12	Lenna	Modern Breed	Border Collie	Female	7	Herding Livestock
13	Luna	Modern Breed	Labrador Retriever	Female	3.1	None
14	Keji	Modern Breed	Sprint Racing Alaskan Sled	Male	3.7	Sprint Sled Dog Racing
15	Kopi	Pre-Modern	New Guinea Singing Dog	Female	1.5	Barn Hunt
16	Romain	Modern Breed	Sprint Racing Alaskan Sled Dog	Male	7.8	Sprint Sled Dog Racing
17	Chichy	Modern Breed	Labrador Retriever	Female	3	Service Work
18	Pasta	Modern Breed	Border Collie	Male	2.08	Herding Livestock
19	PJ	Modern Breed	Labrador Retriever	Male	2.5	Service Work
20	Cue	Modern Breed	Labrador Retriever	Female	2.5	Service Work
21	Kelley	Modern Breed	Labrador Retriever	Male	2.5	Service Work
22	Paisley	Modern Breed	Labrador Retriever	Female	2.3	Service Work
23	Tune	Modern Breed	Labrador Retriever	Female	2.5	Service Work
24	Arbor	Modern Breed	Labrador Retriever	Female	2.6	Service Work
25	Layla	Modern Breed	Labrador Retriever x Golden Retriever	Female	2.4	Service Work
26	Jeanette	Modern Breed	Labrador Retriever	Female	1.5	Service Work
27	Kelbi	Modern Breed	Labrador Retriever	Male	2.6	Service Work
28	Zucch	Modern Breed	Labrador Retriever	Male	1.7	Service Work
29	Odin	Modern Breed	Labrador Retriever	Male	1.7	Service Work

30	Tiff	Modern Breed	Sprint Racing Alaskan Sled Dog	Female	3.9	Sprint Sled Dog Racing
31	Oona	Pre-Modern	Siberian Husky	Female	8	None
32	Kaede	Pre-Modern	Kishu Ken	Male	2.8	Barn Hunt, Weight Pull
33	Amalfi	Modern Breed	Labrador Retriever x Golden Retriever	Female	2.2	Service Work
34	Ramses	Modern Breed	Labrador Retriever	Male	1.9	Service Work
35	Mako	Modern Breed	Sprint Racing Alaskan Sled Dog	Male	1.3	Sprint Sled Dog Racing
36	Shark	Modern Breed	Spring Racing Alaskan Sled Dog	Male	8.2	Sprint Sled Dog Racing
37	Tok	Modern Breed	Sprint Racing Alaskan Sled Dog	Male	3.2	Sprint Sled Dog Racing
38	Vanda	Modern Breed	Border Collie	Female	8.4	None
39	Cap	Modern Breed	Border Collie	Male	11	Herding Livestock
40	Dude	Modern Breed	Labrador Retriever	Male	1.1	Scent Detection
41	Sage	Modern Breed	Labrador Retriever	Female	1.1	Scent Detection
42	Iris	Modern Breed	German Shepherd	Female	2.3	Guide Work
43	Julep	Modern Breed	German Shepherd	Female	2.3	Guide Work
44	Lulu	Modern Breed	German Shepherd	Female	2.2	Guide Work
45	Sakura	Pre-Modern	Kishu Ken	Female	1.8	Barn Hunt, Weight Pull
46	Edgar	Modern Breed	Labrador Retriever	Male	0.9	Scent Detection
47	Jesse	Modern Breed	Labrador Retriever	Male	0.9	Scent Detection
48	Vauk	Modern Breed	Labrador Retriever	Female	1.8	Scent Detection
49	Levi	Modern Breed	German Shepherd	Male	2.4	Guide Work

50	Parrow	Modern Breed	German Shepherd	Male	2.3	Guide Work
51	Raella	Modern Breed	German Shepherd	Female	1.9	Guide Work
52	Saber	Modern Breed	German Shepherd	Male	1.9	Guide Work
53	Buck	Modern Breed	German Shepherd	Male	1.8	Protection Work, Service Work
54	Dak	Modern Breed	German Shepherd	Male	3.8	Protection Work
55	Fern	Modern Breed	Border Collie	Female	4.3	Herding Livestock
56	Wren	Modern Breed	Border Collie	Female	3.5	Herding Livestock
57	Amadeus	Modern Breed	German Shepherd	Male	5.8	Protection Work
58	Pru	Modern Breed	German Shepherd	Female	2.1	Protection Work
59	Billy	Modern Breed	Labrador Retriever	Male	8.8	Hunting Fowl
60	Faren	Modern Breed	German Shepherd	Female	4.8	Protection Work
61	Tamsin	Modern Breed	American Pit Bull Terrier x Australian Shepherd x American Staffordshire Terrier x Labrador Retriever x Boxer x Rottweiler x American Bulldog x Bullmastiff x Boston Terrier	Female	7.3	None
62	Boston	Modern Breed	Labrador Retriever	Female	1.7	Scent Detection
63	Lambert	Modern Breed	Labrador Retriever	Male	0.8	Scent Detection
64	Mark	Modern Breed	Labrador Retriever	Male	1.3	Scent Detection
65	Blizzard	Modern Breed	Labrador Retriever	Female	0.6	Rally
66	Yelena	Pre-Modern	Samoyed	Female	1.4	None

67	Sugar	Pre-Modern	Indian Village Dog	Female	3.5	None
68	Bono	Modern Breed	Labrador Retriever	Male	0.6	Rally
69	Argus	Modern Breed	Labrador Retriever	Male	0.8	Scent Detection
70	Joe	Modern Breed	Labrador Retriever	Male	1.3	Scent Detection
71	Rio	Modern Breed	Labrador Retriever	Male	0.8	Scent Detection
72	Max	Modern Breed	Labrador Retriever	Male	1.8	None
73	Polka	Modern Breed	Labrador Retriever	Female	4.4	None
74	Ryan	Modern Breed	Labrador Retriever	Male	5.2	None
75	Sophie	Modern Breed	Labrador Retriever	Female	1.3	None
76	Milktea	Pre-Modern	Shiba Inu	Female	3.3	None
77	Caroline	Modern Breed	Labrador Retriever	Female	5.7	None
78	Daisy	Modern Breed	Labrador Retriever	Female	4.7	None
79	Sally	Modern Breed	Labrador Retriever	Female	3.7	None
80	Coco	Modern Breed	Labrador Retriever	Female	4	None
81	Joseph	Modern Breed	Labrador Retriever	Male	2.5	None
82	Tatanka	Pre-Modern	Siberian Husky	Male	2.9	None
83	Tuktuk	Pre-Modern	Siberian Husky	Male	5.8	None
84	Jade	Pre-Modern	Korean Village Dog	Female	8.8	Agility
85	Zeeba	Pre-Modern	Saluki	Male	8.6	None

Supplemental Table 16. Demographic data for all subjects in the study.

Cluster Index	Voxels	Maximum T-statistic	x	y	z
1	2976000	5.99	22	69	59
		5.92	19	72	52
		5.82	34	92	79

		5.34	81	70	30
		5.32	93	109	76
		5.31	104	90	75

Supplemental Table 17. Coordinates of significant voxels associated with expansion in modern breed dogs 23 compared to pre-modern dogs (Figure 11). Aligned with the canine brain atlas created by Johnson et al. (2020).

Cluster Index	Voxels	Maximum T-statistic	x	y	z
1	2976000	6.4	87	104	17
		5.85	45	99	16
		5.83	82	87	19
		5.81	38	103	14
		5.57	79	99	19
		5.42	40	106	44

Supplemental Table 18. Coordinates of significant voxels associated with expansion in pre-modern dogs 27 compared to modern breed dogs (Figure 12). Aligned with the canine brain atlas created by 28 Johnson et al. (2020).

Cluster Index	Voxels	Maximum T-statistic	x	y	z
8	75210	6.5	22	72	66
		6.5	22	72	66
		6.47	25	100	71
		6.22	21	69	61
		6.21	42	53	85
		6.19	18	72	49
		5.82	52	62	61
7	33180	7.22	82	87	87

		7.22	82	87	87
		5.98	90	52	83
		5.92	86	51	84
		5.53	101	89	74
		4.87	71	31	73
		4.6	100	72	67
6	2932	4.53	57	117	42
		4.53	57	117	42
		4.35	68	117	38
		2.58	66	126	44
		2.35	46	112	54
5	1179	4.68	79	116	26
		4.68	79	116	26
		4.32	78	114	31
		4.32	78	116	30
		3.84	72	98	29
		3.58	73	102	27
		3.57	72	106	26
4	940	4.93	82	73	29
		4.93	82	73	29
		4.87	82	75	28
		4.15	82	75	31
		4.05	86	78	27
3	554	5.31	77	136	58
		5.31	77	136	58
		4.11	79	131	50
2	210	3.12	96	114	53
1	5	2.72	65	129	44

Supplemental Table 19. Coordinates of significant voxels positively associated with brain weight (see Figure 13). Aligned with the canine brain atlas created by Johnson et al. (2020).

Cluster Index	Voxels	Maximum T-statistic	x	y	z
8	75210	6.5	22	72	66
		6.5	22	72	66
		6.47	25	100	71
		6.22	21	69	61
		6.21	42	53	85
		6.19	18	72	49
		5.82	52	62	61
7	33180	7.22	82	87	87
		7.22	82	87	87
		5.98	90	52	83
		5.92	86	51	84
		5.53	101	89	74
		4.87	71	31	73
		4.6	100	72	67
6	2932	4.53	57	117	42
		4.53	57	117	42
		4.35	68	117	38
		2.58	66	126	44
		2.35	46	112	54
5	1179	4.68	79	116	26
		4.68	79	116	26
		4.32	78	114	31
		4.32	78	116	30
		3.84	72	98	29
		3.58	73	102	27

		3.57	72	106	26
4	940	4.93	82	73	29
		4.93	82	73	29
		4.87	82	75	28
		4.15	82	75	31
		4.05	86	78	27
3	554	5.31	77	136	58
		5.31	77	136	58
		4.11	79	131	50
2	210	3.12	96	114	53
1	5	2.72	65	129	44

Supplemental Table 20. Coordinates of significant voxels negatively associated with brain weight (Figure 13). 35 Aligned with the canine brain atlas created by Johnson et al. (2020).

Cluster Index	Voxels	Maximum T-statistic	x	y	z
11	8977	7.21	83	100	10
		7.13	91	103	18
		6.49	90	82	17
		5.8	93	91	26
		4.44	83	122	28
		3.62	82	106	44
10	5583	6.16	32	96	9
		6.06	42	99	11
		5.69	33	83	17
		5.22	39	86	14
9	1743	8.03	60	86	36
		6.95	62	94	31
		5.28	61	107	41
		4.97	60	72	43
		4.93	64	106	45
		4.37	66	102	45
8	1087	4.66	76	24	38
		4.64	70	23	50
7	583	5.17	73	54	45
		4.45	69	61	35
		4.25	71	59	39
		3.83	63	63	32
		3.79	63	65	33
		3.67	67	58	31
6	342	4.66	86	47	23
5	129	3.68	97	37	32
4	111	4.86	53	56	46
3	102	4.3	74	44	15
2	56	3.65	87	28	32
		3.64	87	29	30
		3.54	87	30	28
		3.5	88	27	36
1	39	4.02	93	37	48

Supplemental Table 21. Coordinates of significant voxels negatively associated with brain weight (Figure 13). 35 Aligned with the canine brain atlas created by Johnson et al. (2020).

Cluster Index	Voxels	Maximum T-statistic	x	y	z
3	2139	4.81	93	110	77
		4.8	85	112	75
		4.53	94	113	78

		4.51	88	94	77
		4.35	94	116	77
		4.31	93	118	77
2	132	4.91	79	150	39
1	6	4.43	43	143	48

Supplemental Table 22. Coordinates of significant voxels positively associated with expansion in modern breed 38 dogs compared to pre-modern dogs, after controlling for brain weight (Figure 14). Aligned with the 39 canine brain atlas created by Johnson et al. (2020).

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